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POLYPS OF THE RECTUM AND COLON IN INFANTS AND IN CHILDREN

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Although it is true that the great majority of polyps of the rectum and colon are either adenomatous or adenocarcinomatous, some are sarcomatous; and others are fibrous, myxomatous, lipomatous, angiomatous or inflammatory. The term polyp as applied to lesions of the rectum and colon should therefore be considered as a general designation which applies to the form or the shape of the lesion rather than to its histologic or pathologic type.

Because of the relative rarity of polyps of the rectum and colon in infants and children, there are few articles in the literature which deal with the variability of the lesions with respect to number and situation, the different histologic appearances which they may exhibit and the diagnostic and therapeutic problems which they may offer.

There are no informative statistics regarding the incidence of polyps among infants and children. Pennington [1] stated that adenomatous polyps are observed with relative frequency in young infants, but he did not give any figures with respect to the frequency which can be confirmed. He cited Bokay [2] as having stated that he had observed 25 instances of adenoma of the rectum in children. He also cited the statement of Jacobi [3] to the effect that he had seen about 100 patients with polyps, most of whom were from 2 to 5 years of age, and that he had observed 3 or 4 such patients each year. Diamond [4] in 1939 reported the case of a girl aged 30 months who had two adenomas in the rectum. In the literature he was able to find reports of 24 cases which he considered were comparable to his own. One of the cases which he included

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1. Pennington, J. R.: A Treatise on the Diseases and Injuries of the Rectum, Anus and Pelvic Colon, Philadelphia, P. Blakiston's Son & Co., 1923, p. 484.

2. Bokay, cited by Pennington.[1]

3. Jacobi, cited by Pennington.[1]

4. Diamond, M.: Adenoma of the Rectum in Children: Report of a Case in a Thirty Month Old Girl, Am. J. Dis. Child. **57**:360-367 (Feb.) 1939.

in his review was reported by Weber and myself.[5] Diamond referred to this case as the single instance in which an adenoma of the colon had undergone malignant degeneration. Whether we stated that the lesion was an adenocarcinoma or that the lesion had undergone "adenocarcinomatous degeneration" must be left to the reader's interpretation of the statements in the article. Diamond's report serves to call attention to the fact that differences in pathologic interpretation tend to color the reports of various authors. Thus, in a report by Dewis [6] there is an account of 101 cases of rectal lesions. Of these lesions, 2 were angiomas, 2 fibromas, 10 myomas, 6 lipomas and 81 adenomas. Even if the ages of the patients are disregarded, such a histologic distribution of the lesions would be quite out of line with that which my associates and I have observed at the Mayo Clinic, but it is possible that many of the lesions which were diagnosed as adenomas we should have designated adenocarcinomas. The data of Lawrence [7] tend to bear out this difference in pathologic interpretation. He found polyps of the gastrointestinal tract in 3.3 per cent of 7,000 cases in which necropsy was performed. Of these polyps, 6.5 per cent were found to have undergone "malignant transformation," and other accompanying lesions which were frankly carcinomatous were observed in an additional 12 per cent of the cases. These data were presented without mention of the ages of the patients.

There is apparently some difference of opinion regarding the technic to be employed in making a proctoscopic diagnosis in the cases of infants and children, as judged by the statements of Daniels [8] and Paulson,[9] on the one hand, and those of Buie [10] and Smith,[11] on the other. Apparently, the roentgenologic methods of diagnosis advocated by Weber [12] for deter-

5. Kennedy, R. L. J., and Weber, H. M.: Polyposis of the Colon in Children, Am. J. Dis. Child. **42**:69-76 (July) 1931.

6. Dewis, J. W.: A Small Fibroma of the Ileum Resulting in Obstruction of the Bowel, with a Consideration of Various Forms of Benign Intestinal Tumors, Boston M. & S. J. **155**:427-433 (Oct. 18) 1906.

7. Lawrence, J. C.: Gastrointestinal Polyps: Statistical Study of Malignancy Incidence, Am. J. Surg. **31**:499-505 (March) 1936.

8. Daniels, E. A.: Rectal Disorders in Childhood, Am. J. Dis. Child. **54**:573-589 (Sept.) 1937.

9. Paulson, M.: Rectosigmoidoscopy in Infancy and in Childhood: A Nonsurgical Procedure; Indications, Instruments, Technic and Appearance of the Distal Part of the Colon, Am. J. Dis. Child. **52**:1430-1444 (Dec.) 1936.

10. Buie, L. A.: Practical Proctology, Philadelphia, W. B. Saunders Company, 1938.

11. Smith, N. D.: Rectal Polyps in Infancy, S. Clin. North America **14**:713-715 (June) 1934.

12. Weber, H. M.: A Method for the Roentgenologic Demonstration of Polypoid Lesions and Polyposis of the Colon, Proc. Staff Meet., Mayo Clin. **5**:326-327 (Nov. 12) 1930.

mining the presence of lesions of the colon beyond the range of the sigmoidoscope are not generally employed. In this report it is to be understood that the lesions were identified in the section on proctology of the Mayo Clinic, which is in charge of Dr. Buie, or in the section on roentgenology, by the method of Dr. Weber.

During the years 1925 to 1940, inclusive, at the Mayo Clinic, 49 infants and children with polyps of the rectum and colon were observed. The patients ranged in age from 6 months [13] to 13 years. Nearly half

TABLE 1.—*Age of the Patient in Forty-Nine Cases of Polyps of the Colon and Rectum in Infants and Children*

Age, Years	No. of Patients
0 to ½	1
1	1
2	6
3	2
4	12
5	6
6	5
7	3
9	2
10	4
11	2
12	3
13	2

TABLE 2.—*Chief Symptoms in Forty-Nine Cases of Polyps of the Colon and Rectum in Infants and Children*

Symptom	No. of Cases
Blood in stool	43
Diarrhea	8
Mucus in stool	7
Protruding mass	14
Painful defecation	2
Abdominal pain	13
Difficult defecation	1
Spontaneous expulsion of polyp	1
None	2

of the patients were 4, 5 or 6 years of age when they were first seen at the clinic. There is no explanation of the preponderance of patients of these ages (table 1). Of the 49 patients, 30 were boys and 19 girls.

The chief symptoms were bleeding from the bowel, abdominal discomfort, a mass protruding from the anus and diarrhea. Less frequently, the presence of mucus in the stools, painful or difficult defecation and spontaneous expulsion of a polyp were noted (table 2). The bleeding was intermittent, and more than a teaspoon of blood was never passed at one time. The blood was usually on the outside of the stool. In some cases blood was noted nearly every day; in others periods of a month or

13. The case of the patient aged 6 months was reported in detail by Smith.[11]

more might pass without any being seen. In the cases in which there was some protrusion, the interpretation usually made by the parents or the physician was prolapse of the bowel. This can be readily understood, since the covering of the polyp resembles the mucous membrane of the bowel. Abdominal pain was seldom severe and was most prominent in cases in which polyps were present in parts of the large bowel other than the rectum or the sigmoid. Diarrhea was seldom marked, and usually not more than three or four stools were passed daily. There was not much departure from normal so far as consistency or color of the stools was concerned. There was seldom any excess of mucus noted, except in 3 cases in which diffuse polypoid disease involved the entire bowel and in 2 cases in which chronic ulcerative colitis was present. Two of the 3 cases of diffuse polypoid disease were reported previously by Weber

TABLE 3.—*Duration of Chief Symptoms in Forty-Nine Cases of Polyps of the Colon and Rectum in Infants and Children*

Duration	No. of Cases
Not more than 1 day	1
1 day to 1 week	1
1 to 4 weeks	4
1 to 5 months	4
6 months to 1 year	9
1 to 2 years	11
2 to 3 years	7
3 years	2
4 years	1
5 years	1
6 years	4
7 years	1
No record	3

and me.[5] The symptoms were not such as to be readily confused with those caused by chronic ulcerative colitis, tuberculous enteritis, amebic colitis or bacillary dysentery.

Symptoms had been present for variable periods. In 1 instance bleeding and protrusion had been noted for only one day. In other cases the symptoms had been present for periods as long as seven years. The great majority of the patients were seen after symptoms had been present for six months to three years (table 3).

In some cases the presence of a polyp or polyps could be readily determined by digital examination of the rectum. However, in all but 1 case proctoscopic examination was the essential procedure by which polyps of the rectum and the sigmoid were diagnosed. In 30 cases only one polyp was found in the rectum (table 4). In other cases from two to seven polyps were visualized by means of the proctoscope. In 3 cases of diffuse polypoidosis the polyps were innumerable, as determined by proctoscopic and roentgenologic examination. In 2 cases of chronic

ulcerative colitis so-called pseudopolyps were seen. One patient, a child 4 years of age, died suddenly, of other causes. There was no history suggesting the presence of a lesion of the large bowel, but at necropsy a polyp, measuring 3 by 1.7 by 1.5 cm., was found in the descending colon.

Roentgenologic examination was made in 32 of the 49 cases. Such examination was not carried out in all cases because the technic necessary for the demonstration of the lesions had not been perfected when some of the patients were observed and polyps of the rectum and colon cannot be discovered by roentgenologic examination made after the administration of an ordinary barium enema. In the cases in which roentgenologic examination was carried out the results were as follows: In 15 cases polyps were found in the rectum but the colon was normal; in 6 cases one polyp was found in the colon, and in 1 case 3 polyps of the colon were found. Numerous polyps were present in 1 case, and in 3 cases the

TABLE 4.—*Number of Rectal Polyps Disclosed by Proctoscopic Examination in Forty-Eight* Cases of Polyps of the Colon and Rectum in Infants and Children*

No. of Rectal Polyps	No. of Cases
None (polyps of colon only)	4
One	30
Two	3
Three	3
Four	2
Seven	1
Innumerable	3
Chronic ulcerative colitis with polyps	2

* Proctoscopic examination was not performed in 1 of the 49 cases considered in this paper.

polyps were innumerable. In each of 4 cases in which proctoscopic examination failed to disclose any polyps, roentgenologic examination revealed a polyp in the colon. In the 2 instances of chronic ulcerative colitis with pseudopolyps, the lesions were demonstrated roentgenographically.

The treatment naturally varied according to the site and the number of the lesions present. In 27 cases fulguration through the proctoscope without any other form of treatment sufficed to destroy the polyps. Excision alone was employed in 1 case, and ligation was done in 2 cases. In 2 cases in which there were lesions in the colon only, transcolonic excision was performed. Fulguration together with transcolonic excision was carried out in 3 cases in which there were polyps in both the rectum and the colon. Fulguration and segmental resection were employed in 2 cases in which there were polyps in the rectum and more than one polyp in the colon.

One patient had diffuse polypoid disease of the colon. He first came to the clinic in 1933, when he was 12 years of age. At that time, exam-

ination of a specimen of a polyp obtained by means of the proctoscope disclosed adenocarcinoma grade 2. An effort was made to fulgurize the polyps in the rectum, but this was unsuccessful because of lack of cooperation. The patient returned to the clinic in 1939, when he was 18 years of age. In addition to innumerable polyps, there was a large carcinoma beginning 10 cm. above the anus and involving the anterior two thirds of the lumen of the bowel. A single barrel ileostomy was performed. It was planned to perform complete colectomy followed by fulguration of the rectal polyps. The colectomy was performed, but the patient died after the operation. Fulguration and roentgen therapy were carried out in 1 case in which there were several polyps in the rectum and several more at various points in the colon. In 1 case in which a roentgenologic diagnosis of polyp of the colon had been made, such a lesion was not demonstrated at operation. No treatment for the polyps was employed in 9 cases. Two of these were the instances of diffuse polypoidosis previously reported, and 2 were cases of chronic ulcerative colitis, and in 1 case a polyp was found at necropsy. In the other 4 cases treatment was refused.

Because many of the polyps were removed by fulguration, which has been found to be most satisfactory in treating polyps of the rectum, it is frequently not possible to obtain tissue for a satisfactory pathologic diagnosis. However, tissue was obtained in 18 of the 49 cases. In 8 of these cases the diagnosis was adenoma, in 8 adenocarcinoma grade 1, in 1 adenocarcinoma grade 2 and in 1 reticulum cell type of lymphosarcoma.

COMMENT

There has been a considerable amount of controversy regarding the cause of such polyps. That there is a hereditary factor in diffuse polypoid disease is now generally accepted. Buie has considered the arguments for and against a hereditary factor in all cases of neoplastic polyps. He also has outlined the pathogenesis of the so-called pseudopolyps of chronic ulcerative colitis. The reader is referred to his works.[14]

In a case in which an infant or a child has bleeding from the bowel, polyps must be considered as a possible cause. The services of a competent proctologist and roentgenologist are essential for determining whether such lesions are present. Large, pedunculated polyps are easily visualized by proctoscopic and roentgenologic examination. Difficulty is offered, however, by the smaller lesions, some of which may be only a few millimeters in diameter. The shape of the lesion, that is, whether it is pedunculated or sessile, also determines to a great extent the ease of recognition. Small sessile polyps, although seen relatively

14. Rankin, F. W.; Bargen, J. A., and Buie, L. A.: The Colon, Rectum and Anus, Philadelphia, W. B. Saunders Company, 1932. Buie.[10]

easily through the proctoscope, may not be visualized by roentgenologic examination. Instances are known in which partial resection of the colon has been carried out to eradicate one, two or several polyps but in the resected portion of the bowel other small sessile lesions were found. In some cases these consisted of little more than small regions of hyperplasia of the mucosa. Yet such polyps must be considered to possess the same potentialities for growth and carcinomatous degeneration as do the large lesions, which are easily visualized.

Another difficulty which confronts the roentgenologist who is asked to determine the presence or absence of polyps in the colon of a young patient is the partial or total lack of cooperation on the part of the patient. Needless to say, much time must be spent to obtain the confidence and cooperation of some of them in order that the examination may be satisfactory. It is imperative, however, that roentgenologic examination should be performed in every case in which proctoscopic examination has demonstrated the presence of a polyp in the rectum or colon of an infant or a child. This is even more imperative in cases in which children have had unexplained bleeding from the bowel but proctoscopic examination has failed to disclose any abnormality.

The outlook for young patients who have polyps of the rectum and colon depends on several factors. In order that they may be relieved of symptoms, it is necessary that all the lesions be completely destroyed or removed. In cases in which the polyps have an inflammatory basis, no immediate treatment may be indicated. In cases in which there are only one or a few polyps, which have been diagnosed by proctoscopic and roentgenographic examination, removal or destruction is rather simple. In cases of multiple polypoid disease, total resection of the colon and fulguration of the rectal polyps, as advocated by Mayo and Wakefield,[15] is the best method of treatment so far devised, although it involves a high risk. As was pointed out by Dixon,[16] if frank clinical carcinoma has developed, preliminary ileostomy followed by resection of the colon and of the rectum, too, is the usual order of procedure.

Although knowledge of the exact histologic structure of the polyps is desirable, the evidence of malignant potentialities is sufficient to warrant removal of all of them, whenever found. The histologic evidence of malignancy encountered in this series of cases substantiates the recommendations of Bargen.[17]

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15. Mayo, C. W., and Wakefield, E. G.: Disseminated Polyposis of the Colon: A New Surgical Treatment in Selected Cases, J. A. M. A. **107**:342-347 (Aug. 1) 1936.

16. Dixon, C. F.: The Surgical Treatment of Single and Multiple Polyps of the Colon and Rectum, Proc. Staff Meet., Mayo Clin. **15**:109 (Feb. 14) 1940.

17. Bargen, J. A.: Inception of Polyps of the Intestine: Their Association with and Relationship to Malignant Disease, Proc. Staff Meet., Mayo Clin. **15**: 105-107 (Feb. 14) 1940.

In all of the cases except the 3 cases of polypoid disease and the 2 cases of chronic ulcerative colitis, polyps which were visualized by proctoscopic and roentgenologic methods were removed. There has been no instance of recurrence which necessitated the return of the patient because of reappearance of the original symptoms.

SUMMARY

Bleeding from the bowel was by far the most common symptom in the cases of 49 infants and children who had polyps of the rectum, the colon or both. The polyps were visualized by proctoscopic and roentgenologic methods. Treatment was by surgical methods or by removal or destruction of the polyps by means of the proctoscope. Some of the lesions were frankly carcinomatous. All adenomatous polyps, except those found in certain cases of chronic ulcerative colitis, have carcinomatous potentialities and should therefore be removed or destroyed.

THE GRANULES IN THE LEUKOCYTES IN GARGOYLISM

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Gargoylism is a syndrome characterized by dwarfism, chondrodystrophic skeletal changes, infantilism, a facies resembling that of cretinism, thickening of the skin and the periarticular structures which limit joint extension, splenohepatomegaly and familial recurrence. Cloudy corneas often develop.

The white blood cells occasionally contain a hitherto undescribed type of granulation. This kind of cell has been encountered by my associates and me in 4 of 8 cases of gargoylism. The pathogenesis or significance of the granules (illustration) is unknown. They are found only in the white blood cells and occur much more often in the polymorphonuclears than in the lymphocytes or the monocytes. They are larger than the granules which are normally present in cells, are more numerous and usually are a dark lilac color when stained by the Giemsa-Wright technic. On other occasions, even in cells from the same patient, they may be much smaller than ordinary granules and may take an eosinophilic stain, but they are not as highly refractile as are typical eosinophilic granules. The cytoplasm stains pink, and occasionally one or two vacuoles are seen, suggesting phagocytosis. Over 90 per cent of the polymorphonuclear cells have a three-lobed nucleus; in the remainder it is two lobed. A nucleus with four or five lobes is rare. Occasionally an immature white cell appears in the blood. Leukopenia was present in 2 of the 4 cases. A mild hypochromic microcytic anemia may develop. The usual routine hematologic tests (platelet count, bleeding time, clotting time, etc.) reveal nothing abnormal.

Such granules are found in the white blood cells of the sternal marrow and usually in the spleen if the blood stream contains them. In 1 case they occurred only in the spleen, however. While the occurrence of such granulated cells in other hemopoietic sites has been suspected, it has not been thoroughly investigated, since no satisfactory studies have been made at autopsy. In the marrow in which such cells

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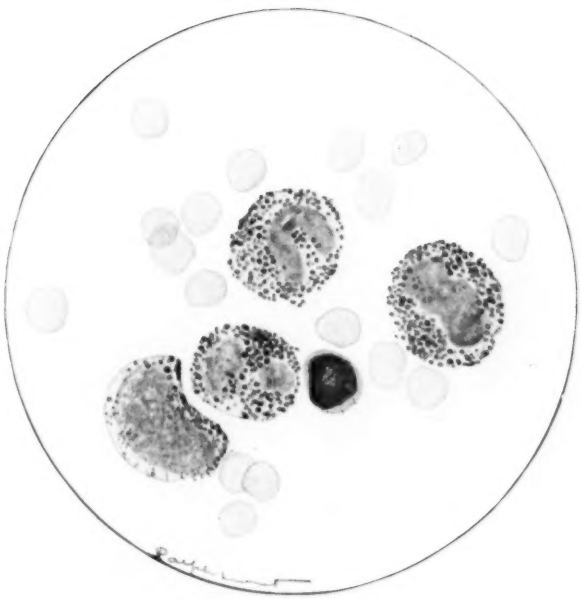
occur the differential count is changed toward a leukogenic reaction, both by an increase in myeloid cells, especially segmented neutrophils containing the type of granule discussed here, and by a decrease in erythrogenic cells. Neither biopsy of tonsils in 2 cases and of skin in 1 case nor autopsy in 2 cases revealed this type of cell. The granulated white cells occurred in the blood in 1 case in which the gargoylism was fatal. The other tissues were neither properly preserved nor stained for observation of such cells. Sternal marrow and blood were examined for this type of granulated white cell in 4 cases, in 3 of which such cells were found. In 1 of the 3 cases similar cells were found in the spleen. As has already been mentioned, in 1 other case the cells were absent from the blood and bone marrow and occurred in the spleen alone.

The percentage of such granulated cells fluctuates, but usually 60 to 90 per cent of the polymorphonuclears, and as much as 20 to 25 per cent of the total number of white cells are of this type. The differential white cell count suggests a tendency toward lymphocytosis. During infection the number of polymorphonuclears, and hence of the granulated cells, rapidly increases. In size the granules vary from fine dust to large, coarse particles.

In 4 patients analysis of the blood also revealed a tendency toward fat storage in that the cholesterol (220 to 310 mg. per hundred cubic centimeters) was high and the total fat and fatty acids were slightly elevated. The phospholipids were normal. In 1 patient whose blood was examined for kerasin, phrenosin and cerebrosides, the results were negative. Some or all of the following determinations were done on the blood at various stages of the disease and repeated, with normal results in all 8 cases: calcium content, phosphorus content, Wassermann reaction, van den Bergh reaction, icteric index, urea content, dextrose tolerance, chloride content, bromsulphalein retention and sedimentation rate. The cause of the fat retention was not determined. The retained substance may prove to be a cerebroside-phosphatide.

Since these granules were first observed (1930), there has been much speculation about their cause and nature. Perhaps they are toxic granules, but there is no certain procedure to prove this hypothesis. Their relation to fat retention has commanded attention since Washington [1] appended the term lipochondrodystrophy to gargoylism. The

1. Washington, J. A.: Lipochondrodystrophy, in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1937, vol. 4, chap. 30.



Toxic granules occurring in the white cells in cases of gargoylism.

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description by Kressler and Aegerter [2] of a lipid-like substance observed in various tissues at autopsy is arresting evidence. Could this lipid storage be a complication rather than a primary cause?

It is not felt that these cells are mast cells. Phagocytosis does not seem likely. Allergy, parasitism, a primary endocrinopathy, leukemia, Gaucher's disease and Niemann-Pick disease have all been ruled out in these 8 cases.

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2. Kressler, R. J., and Aegerter, E. E.: Hurler's Syndrome (Gargoylism): Summary of Literature and Report of Case with Autopsy Findings, J. Pediat. **12:** 579-591 (May) 1938.

EFFECT OF REFINED ANTIPERTUSSIS RABBIT SERUM ON THE HUMORAL ANTIBODY TITER IN PERTUSSIS

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Recently, considerable interest has developed in passive immunization against pertussis. In this respect, adult immune serum, convalescent serum and hyperimmune human serum have received particular attention. The last type of serum is protective against the experimental murine disease.[1] When injected in doses varying from 10 to 40 cc. it also increases the opsonocytophagic reaction and the agglutinating titer of the blood of infants.[2] Moreover, recent preliminary reports [3] have indicated that the administration of hyperimmune human serum is effective in preventing or modifying the disease in infants exposed to pertussis.

Because of the apparent limitations that may exist in large scale production of hyperimmune serum, effective as it may be, our attention has been directed to the investigation of the value of immune rabbit serum. An immune serum prepared by injecting suspensions of living organisms into rabbits was found to protect mice against the experimental

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1. Bradford, W. L., and Wold, M.: Effect of Hyperimmune Human Serum (Lyophile) and of Sulfapyridine on Experimental Murine Pertussis, Am. J. Dis. Child. **58**:1228 (Dec.) 1939.

2. Katsampes, C.; McGuinness, A. C., and Bradford, W. L.: Effect of Hyperimmune Human Serum (Lyophile) on the Humoral Antibody Titer in Pertussis, Am. J. Dis. Child. **58**:1234 (Dec.) 1939.

3. (*a*) Kendrick, P.: A Note on the Use of Reinforced Convalescent or Hyperimmune Serum for Passive Immunization of Infants Exposed to Pertussis, J. Pediat. **9**:118, 1936. (*b*) McGuinness, A. C.; Bradford, W. L., and Armstrong, J. G.: The Production and Use of "Hyperimmune" Human Whooping Cough Serum, ibid. **16**: 21, 1940. (*c*) Cohen, P., and Lapin, J.: Prophylaxis Against Whooping Cough in Exposed Children with Special Reference to Serum, ibid. **15**:78, 1939.

disease.[4] The globulin fraction of this serum, prepared by precipitation with sodium sulfate, was found to be equally protective, although it contained but one third of the nitrogen content of the original serum.

The present paper describes the effect of antipertussis rabbit serum on the humoral antibody titer of infants when injected intramuscularly during the early stage of the disease.

METHOD

The immune rabbit serum used in the present experiments was obtained from Dr. W. E. Bunney, of E. R. Squibb & Sons. He has supplied the following account of its mode of preparation: "The serum was obtained from hyperimmunized rabbits and was concentrated by ammonium sulfate fractionation. The concentrated serum had a potency of at least 2,000 units when tested in comparison with a provisional standard serum on mice given intramuscular injections of the serum dilutions one hour before intraperitoneal injection of pertussis organisms suspended in mucin. The potency of the provisional standard was established by calling 1 unit the amount of serum which protected 50 per cent of the mice against one minimal lethal dose of pertussis organisms suspended in mucin."

The patients selected to receive injections of the serum were 13 infants admitted to the hospital during the early stages of pertussis. Their ages varied from 4 weeks to 2 years. Six of the infants were in the first week of the disease; 5, in the second week, and 2, in the third week.

Since the agglutinating titer of the serum against Haemophilus pertussis[5] usually increases during the course of pertussis and since recent reports have described increases in the mouse-protective titer of serum during the course of the disease, it was decided to compare the effects of antipertussis rabbit serum on these two antibodies in the present study.

On admission, material for culture was taken from the nose so that the strain of pertussis might be identified,[6] a complete blood count was made and a sample of venous blood was withdrawn for the titration of antibody. After preliminary testing for sensitivity, each infant was given an intramuscular injection of from 4 to 7 cc. of serum. Forty-eight hours later a second sample of venous blood was drawn for titration of antibody.

After the strain of H. pertussis isolated from each infant was identified, it was cultured on Bordet's medium so that suspensions of the organism might be prepared for testing the agglutinating and mouse-protective titers of the patient's serum before and after the injection of immune rabbit serum. In this manner it was possible to test the serum of each patient against the homologous strain of

4. Scherp, H. W.; Bradford, W. L., and Wold, M.: Protective Value of Immune Rabbit Serum and Its Globulin Fraction Against Experimental Murine Infection with Hemophilus Pertussis, Proc. Soc. Exper. Biol. & Med. **42**:172, 1939.

5. (*a*) Mishulow, L.; Klein, I. F.; Liss, M. M., and Leifer, L.: Protection of Mice Against H. Pertussis by Serum: Comparison of Protection with Agglutination, J. Immunol. **37**:18, 1939. (*b*) North, E. A.; Keogh, E. V.; Anderson, G., and Williams, S.: Passive Immunity in Experimental Pertussis, Australian J. Exper. Biol. **17**:275, 1939.

6. Bradford, W. L., and Slavin, B.: Nasopharyngeal Cultures in Pertussis, Proc. Soc. Exper. Biol. & Med. **43**:590, 1940.

H. pertussis in every instance except 3. The serum of 1 of these 3 infants was tested against a strain isolated from a sibling; hence, in all probability it was identical with his own strain. It was possible to compare the results obtained for patient C. G. and those for his identical twin, A. G.

The agglutination tests were carried out according to the rapid method described by Kendrick.[7]

The mouse-protective value of the serums was tested by a recently described method,[8] the essential features of which follow. To test the protective value of the serum of each patient 90 mice were used: 30 to test each of the two serums and 30 to determine the minimal lethal dose of the organism. A suspension was prepared by scraping the seventy-two hour growth from the surface of a Bordet medium plate into a 0.85 per cent solution of sodium chloride. After mixing and filtering through cotton, the suspension was diluted to match the turbidity of a known suspension of H. pertussis containing 10,000,000,000 organisms per cubic centimeter. Each serum was tested in the following strengths: undiluted, 1:4, 1:16, 1:64 and 1:256. To the various dilutions of serum an equal volume of the bacterial suspension containing 5,000,000,000 organisms per cubic centimeter was added. After shaking, the mixture was incubated for thirty minutes in a water bath at 37 C. (98.6 F.).

White Swiss mice, 3 weeks of age, were anesthetized by placing them in a glass jar containing a small bit of cotton saturated with a mixture of 1 part of chloroform and 2 parts of ether. When the animal was completely relaxed, 0.05 cc. of the serum-organism mixture was carefully dropped into the nostrils. Six mice were infected with each dilution of serum. After inoculation the mice were kept in small groups at a temperature of 20 to 22 C. (68 to 71.6 F.).

The method described was found to give results comparable with those obtained when the mouse received the serum intra-abdominally and the organisms intranasally. A practical advantage of the method is that a much smaller amount of serum is necessary to make a test.

To determine the minimum lethal dose dilutions of the bacterial suspension were made so that the infecting doses for each five groups (consisting of 6 mice each) contained 250,000,000, 62,500,000, 15,600,000, 3,900,000 and 970,000 organisms, respectively. The mice were observed throughout a ten day period after inoculation. The number of deaths occurring on each day was recorded. The minimum lethal dose was calculated by determining the dose of organisms which killed 50 per cent of the 30 animals during the ten day period.

RESULTS

The results obtained by comparing the mouse-protective titers of the serums taken before and forty-eight hours after the administration of immune rabbit serum are shown in table 1, as are the differences in the agglutinating titers of these serums and the minimum lethal dose of the strain used in each titration.

It may be seen that a definite increase in the mouse-protective value of the serum of each infant occurred as a result of receiving the immune

7. Kendrick, P.: Rapid Agglutination Technic Applied to B. Pertussis Agglutination, Am. J. Pub. Health **23**:1310, 1933.

8. Scherp, H. W.; Bradford, W. L., and Slavin, B.: Titration of Antipertussis Sera by Passive Protection Tests in Mice, to be published.

rabbit serum. This increase varied from two and a half fold (J. H.) to one hundred and seventy-seven fold (J. P.). It is of interest that the serum of each of the infants had some protective value before the antibody solution was administered. This protective value, expressed as the number of minimum lethal doses against which 0.025 cc. of undiluted serum gave protection, varied from 1.5 (J. Pi.) to 869 (H. R.). In each instance the serum possessed an agglutinating titer of 1:20.

TABLE 1.—*Humoral Antibody Titers of Thirteen Infants with Pertussis Treated with Immune Rabbit Serum**

Case	Patient	Amount of Serum Injected, Cc.	Minimum Lethal Dose, Millions of Organisms	No. of Minimum Lethal Doses Against Which 0.025 Cc. Undiluted Serum Protected		Increase in Protective Titer	Agglutinating Titer	
				Before Serum	After Serum		Before Serum	After Serum
1	R. R.	4	3	42	4,149	98 X	0	320
2	H. R.	7	11‡	869	2,954	3.5 X	20	320
3	J. H.	6	22	5.5	14	2.5 X	0	320
4	J. P.	4	62	2	354	177 X	0	320
5	P. L.	4	27	4.5	111	24 X	0	80
6	S. R.	4	6	28	248	8.5 X	0	160
7	R .G.	5	6§	16	542	33 X	0	80
8	E. S.	6	25	5	118	24 X	0	40
9	V. P.	6	16	8	312	39 X	0	40
10	O. H.	4	1‖	125	2,500	20 X	0	320
11	M. P.	6	130	7	245	36 X	0	160
12	J. Pi.	6	87	1.5	18	13 X	20	640
13	C .G.	6	9	17	576	32 X	0	160
13	C. G.†	..	80	..	56	....	..	160
14	A. G.	No serum	6	20	20	0 X	0	0
14	A. G.†	..	80	..	199			

* The therapeutic serum possessed an agglutination titer of 1:40,000, and 0.025 cc. of it protected mice against from 8,000 to 15,000 minimum lethal doses of the organism.

† C. G. and A. G. were identical twins, tested in the first and the seventh week of the disease; A. G. received no serum.

‡ R. R. strain.

§ S. R. strain.

‖ E. S. strain.

The agglutinating titer of the immune rabbit serum was found to be 1:40,000, and 0.025 cc. of this serum protected mice against from 8,000 to 15,000 minimum lethal doses of the organism.

It is apparent that the agglutinating titers of the infants' serum also increased, ranging from 1:40 to 1:640. In 11 of the 13 infants no agglutinins were present before injection of the rabbit serum. This result was to be expected because of the early stage of the disease at which the infants were tested. There was no correlation between the height of the agglutinating titer of the infants' serum after the treatment with serum and the mouse-protective titer. This observation corroborates the findings of Mishulow and co-workers.[5a]

While the clinical course of the disease in each infant (except 1) was satisfactory, we were naturally unable to prove that it would not have been equally good without administration of the serum. Of the 13 infants treated with immune rabbit serum, 1 died. This patient (S. R.), who was 4 weeks of age, was admitted to the hospital during the second week of the disease, when she had extensive bronchopneumonia. As a result of receiving 4 cc. of immune serum, the protective value of her serum increased from 28 to 248 minimum lethal doses and the agglutinating titer increased from 0 to 1:160. In spite of this apparently good antibody response, death occurred six days later. It is interesting to note

TABLE 2.—*Clinical Data on Thirteen Infants with Pertussis Treated with Immune Rabbit Serum*

Case	Patient	Sex	Age	Week of Disease	Complications	Cc. of Serum Injected	Absolute Mononuclear Cell Count		Course of Disease
							Before Serum	After Serum*	
1	R. R.	M	7 mo.	2d	Otitis media.....	4	15,288	10,696 (7)	Average
2	H. R.	M	2 yr.	3d	Pneumonia.....	7	62,307	37,364 (3)	Severe
3	J. H.	M	7 wk.	2d	Pneumonia.....	6	21,140	13,545 (5)	Severe
4	J. P.	M	3 mo.	2d	Otitis media.....	4	9,758	5,320 (10)	Average
5	P. L.	M	8 mo.	1st	None.....	4	36,800	29,792 (6)	Mild
6	S. R.	F	4 wk.	2d	Pneumonia.....	4	20,000	27,166 (6)	Severe; died
7	R. G.	M	17 mo.	3d	None.....	5	16,900	13,715 (8)	Mild
8	E. S.	M	7 mo.	1st	Otitis media.....	6	26,368	11,200 (7)	Mild
9	V. F.	F	2 mo.	1st	Pneumonia.....	6	9,144	7,475 (15)	Mild
10	C. H.	F	2 mo.	1st	None.....	4	5,964	8,976 (13)	Mild
11	M. P.	F	4 mo.	2d	None.....	6	19,698	6,478 (11)	Mild
12	J. Pi.	M	7 wk.	1st	None.....	6	27,552	9,594 (11)	Mild
13	C. G.†	M	7 mo.	1st	None.....	6	37,060	23,976 (2)	Mild
14	A. G.†	M	7 mo.	1st	None.....	0	15,756	22,496 (2)	Mild

* The figures in parentheses indicate the number of days after injection of the serum the count was made.

† C. G. and A. G. were identical twins, A. G. received no serum.

(table 2) that the absolute mononuclear count of her blood increased from 20,000 to 27,166 during the six days preceding death.

Since it has been suggested [9] that the increase in the absolute lymphocyte count in pertussis may be related to an effect of H. pertussis or its toxin on the hematopoietic system, it was of interest to observe the trend of these cells after injection of the serum. Unfortunately, systematic counts were not made in the present study. Furthermore, the counts which were made were done by various persons. Accordingly, the lymphocytes and the mononuclears have been grouped together, and the values in table 1 represent the absolute mononuclear counts made before

9. (*a*) Tuta, J. A.: A Study of the Lymphocytosis Following Intravenous Injections into Rabbits of Suspensions and Extracts of Hemophilus Pertussis, Folia haemat. **57**:122, 1937. (*b*) Inaba, I., Inamori, S.: Blood Picture in Experimental Whooping Cough, Am. J. Dis. Child. **48**:1193 (Dec.) 1934

and at irregular periods after injection of the serum. It may be significant (table 2) that decreases occurred in the absolute mononuclear counts for 11 of the 13 infants treated. This result is of greater significance, possibly, when it is noted that the majority of these infants were in the first two weeks of the disease, when the lymphocytes ordinarily would be expected to increase rather than to decrease.

For the sake of comparison, we reviewed the records of 16 infants with pertussis (for all of whom culture of material from the nose was positive for H. pertussis) who were observed during the same period as those in the serum-treated group, were of similar ages and were in similar stages of the disease. These 16 infants received only symptomatic treatment, and only 6 showed a corresponding decrease in the absolute mononuclear count.

While the observations on the blood obviously need to be repeated and extended, they suggest that the administration of immune rabbit serum in cases of pertussis may depress the absolute mononuclear count.

Of particular interest were observations made on the twins C. G. and A. G. These 7 month old "single ovum" boys possessed similar facial features and were of the same blood group and probably were identical twins. The disease was equally severe in the 2. C. G. received 6 cc. of immune rabbit serum, while A. G. received only the symptomatic care given to C. G. No difference was noted in the clinical course or in the time of disappearance of the organisms from the upper respiratory tract, as determined by cultures of material from the nose. It was found, however, that the absolute mononuclear count of C. G. fell from 37,060 to 23,976 (table 2) within two days after the injection of serum, while that of A. G., who received no serum, increased from 15,756 to 22,496 during the same period. The mouse-protective titer of the serum of C. G. increased from 17 to 576 (table 1) and the agglutinating titer increased from 0 to 160 as a result of receiving the serum. Samples of A. G.'s serum tested at the same time showed protective titers of 20 and 20 and agglutinating titers of 0 and 0, indicating that there was no increase of these antibodies during the two day interval as a result of the infection with H. pertussis.

Six weeks later, that is, in the seventh week of the disease, the serums of the twins were again tested. At this time the protective value of C. G.'s serum was 56, as compared with 199 for that of A. G. This greater protective value of the serum of A. G., who had received no serum, suggests that it had occurred entirely as a result of stimulation from the disease. The lesser value of the serum of C. G., who had received serum six weeks before, may have occurred as a result of having the process of active immunization interfered with by the administration of specific passive protection. Such interference with the natural produc-

tion of antibodies is known to occur in scarlet fever, for example, when specific antitoxin is administered early in the course of the disease.[10]

Although the data given in the present report do not justify a conclusion as to the therapeutic effect of the administration of immune rabbit serum in pertussis, they suggest that further clinical testing, particularly as regards a possible prophylactic value and the effect of larger doses, should be carried out. Such studies are now in progress.

SUMMARY

The effect of the intramuscular injection of antipertussis rabbit serum on the humoral antibodies of infants with an early stage of pertussis has been observed. In the serum of each of 13 infants given doses of from 4 to 7 cc. of the immune rabbit serum definite increases in the mouse-protective values and the agglutinating titers occurred. Immediate decreases in the absolute mononuclear cell counts of the blood of 11 infants occurred.

10. Davies, J. A. V.: Post Scarlatinal Immunity in Patients Treated with Antitoxin, J. Clin. Investigation **3**:423, 1926.

A STUDY OF THE METABOLISM OF INGESTED PECTIN

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The use of an apple diet and pectin in the treatment of diarrhea raises the question of the fate of pectin in the alimentary tract and the body tissues.[1] How the apple diet or pectin exerts a favorable influence has not been elucidated. It is certain that ingested pectin is decomposed in the alimentary tract of the young adult, since only 10 per cent or less can be recovered from the feces.[2] When pectin is given to a fasting subject, however, less is decomposed; the amount decomposed is influenced, apparently, by the rate of passage through the alimentary tract and perhaps by whether the nitrogen, which is necessary to sustain the organism or organisms involved,[3] is present. The results of experiments on ileostomized human and canine subjects [2c] and the failure of the enzymes in the digestive juices to hydrolyze pectin [4] show that the decomposition of pectin occurs primarily in the colon. Since the secretion of the colon of the dog (and the cat) contains no significant concentration of enzymes,[5] and since we have found that the colonic secretion of the dog does not hydrolyze pectin, the decomposition of pectin in the colon must be due to micro-organisms.

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1. (*a*) The Apple in the Management of Diarrhea in Children, report of the Council on Foods, J. A. M. A. **109**:1636 (Nov. 13) 1937. (*b*) Malyoth, G.: Das Pektin, der Haupttrager der Wirkung bei der Apfeldiät, Klin. Wchnschr. **13**:51, 1934.

2. (*a*) Schneider, E. C.: A Nutritional Investigation of the Insoluble Carbohydrates or Marc of the Apple, Am. J. Physiol. **30**:258, 1912. (*b*) Ehrlich, F.; Imhauser, K., and Voit, K.: Aus der Chemie und Biochemie der Gerüstsubstanzen der Pflanzenzelle, Jahresb. d. schles. Gesellsch. f. vaterl. Kult. **103**:104, 1930-1931. (*c*) Werch, S. C., and Ivy, A. C.: On the Fate of Ingested Pectin, Proc. Soc. Exper. Biol. & Med. **44**:366,1940; Am. J. Digest. Dis. **8**:101, 1941.

3. Murer, H. K., and Crandall, L. A.: Studies on the Absorption of Pectic and Uronic Acids, Am. J. Physiol. **129**:427, 1940. Werch and Ivy.[2c]

4. Kertesz, Z. I.: Pectic Enzymes: V. The Fate of Pectins in the Animal Body, J. Nutrition **20**:289, 1940.

5. Wright, R. D.; Florey, H. W., and Jennings, M. A.: The Secretion of the Colon of the Cat, Quart. J. Exper. Physiol. **28**:207, 1938.

These observations led to a search in the literature for evidence regarding the decomposition products of pectin. When pectin is incubated with a dilute suspension of feces, it is decomposed,[6] with the production of acid.[7] The character of the acids has not been determined. According to Schneider,[2a] reducing substances are not formed when the hemicellulose of "apple marc" is decomposed by a fecal suspension. When partially purified pectin is fermented anaerobically with Granulobacter pectinovorum, butyric acid, a small amount of acetic acid and traces of carbon dioxide are found; and when it is fermented aerobically with Pectinobacter amylophilum, the chief products are carbon dioxide and water and about 2.5 per cent acetic and formic acids.[8] These results probably cannot be applied to the fermentation of pure pectin, since certain organisms which have been reported as fermenting pectin do not ferment pure pectin.[9] The pectinases of molds decompose pectin into galacturonic acid and methyl alcohol,[10] but Saunders and Kertesz [11] reported that the intestinal micro-organisms which hydrolyze pectin also ferment galacturonic acid. It has been concluded on the basis of meager evidence that galacturonic acid is formed and absorbed after the ingestion of pectin,[12] that pectin is metabolized and stored as glycogen [13] and that sufficient methyl alcohol is produced and absorbed to increase the output of formic acid in the urine.[14] However, Imhauser [15] reported that the decomposition products of pectin were not excreted and did not affect the blood sugar and the fatty changes in the liver of phloridzinized dogs, though some decrease in the urinary excretion of acetone bodies was observed.

On the basis of the foregoing observations, it was decided to examine the urine after the ingestion of pectin for galacturonic acid and to

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6. Schneider.[2a] Kertesz.[4]

7. Werch, S. C.; Day, A. A.; Jung, R., and Ivy, A. C.: On the Role of Intestinal Bacteria in the Decmoposition of Pectin, Proc. Soc. Exper. Biol. & Med. **46**:569, 1941.

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10. Kertesz, Z. I.: The Determination of Pectin Methoxylase Activity, J. Biol. Chem. **121**:589, 1937.

11. Saunders, F., and Kertesz, Z. I.: Note on the Fermentation of Pectin and Galacturonic Acid by Intestinal Bacteria, J. Nutrition **20**:289, 1940.

12. Manville, I. A.; Bradway, E. M., and McMinis, A. S.: Pectin as a Detoxication Mechanism, Am. J. Digest. Dis. & Nutrition **3**:570, 1936.

13. Fürth, V. O., and Engel, V.: Verwertung der Pentosane in Tierorganisms, Biochem. Ztschr. **237**:159, 1931.

14. Voit, K., and Friedrich, H.: Ueber das Auftreten von Ameisensäre im Harn bei der Apfeldiät, Klin. Wchnschr. **14**: 1792, 1935.

15. Imhauser, K.: Ueber das Verhalten der Pectine im Stoffwechsel, Arch. f. exper. Path. u. Pharmakol. **167**:589, 1932.

analyze both the urine and the feces for volatile fatty acids and reducing substances, it being kept in mind that these substances might be completely absorbed in the colon. Such determinations should supply data on most of the possible decomposition products of pectin. Of the volatile fatty acids, formic acid is of particular interest, since methyl alcohol is a possible product of its decomposition. Our attention was directed in large measure to the determination of galacturonic acid in the urine. Since pectin is composed of galacturonic acid, the acid is very likely a product of the decomposition of pectin; and if it is absorbed by the colon, it may appear as a galacturonate in the urine. However, before it could serve as a detoxifying agent by forming galacturonates in the liver, as was suggested by Manville, Bradway and McMinis,[12] it must be absorbed. Since it has not been shown whether it is absorbed from the small intestine or the colon, we have undertaken to obtain evidence on that point also.

METHODS

Analysis of Feces and Urine.—Six male medical students were kept on a diet low in crude fiber during a control absorption period. After the control diet had been consumed for four days, 30 Gm. of pectin in gelatin capsules was added to the diet of each subject for four days. Aliquots of feces and urine for analysis were obtained from material secured during the third and fourth days of each period. In the tables, specimen "a" represents material secured on the third day and specimen "b" that secured on the fourth day.

The pectin fed was the pure citrus variety which was used and described in our previous work[2e] and was obtained from the research laboratory of the California Fruit Growers Exchange. This product is essentially free of such impurities as pentoses, pentosans, pigment and other materials frequently found in other pectins.

The control diet consisted of the following: breakfast—200 Gm. of pineapple juice, 2 eggs, 30 Gm. of bacon, 50 Gm. of white bread and 14 Gm. of butter; dinner—90 Gm. of lamb chop, 100 Gm. of potato, 50 Gm. of white bread and 14 Gm. of butter, and supper—200 Gm. of beef steak, 120 Gm. of potato, 50 Gm. of butter and 100 Gm. of ice cream. Coffee was allowed in any quantity at all of the meals.

Ten gram aliquots of thoroughly mixed feces (wet weight), obtained immediately after passage, were used. The material was broken up in a solution containing 20 cc. of normal sulfuric acid and 70 cc. of distilled water, stored in stoppered, sterile bottles, sealed with paraffin and placed in a refrigerator until needed. During the collection of twenty-four hour specimens of urine, 1 cc. of twenty times normal sulfuric acid was added for every 500 cc. of urine. At the end of the period, 100 cc. was measured out and stored in the same way as were the samples of feces. Fresh specimens of urine were measured for volume; the time interval of passage was noted, and they were stored in 100 cc. amounts, as previously described, with 10 cc. of normal sulfuric acid, which was added to prevent bacterial action.[16]

Fresh urine was used for the estimation of galacturonic acid and free reducing substances, and the procedure was carried out the day the specimen was secured. Determinations for total hydrolyzable reducing substances and volatile acids were

16. Friedemann, T. E.: Metabolism of Pathogenic Bacteria: I. Bacteriological and Chemical Methods, J. Bact. **35**:527, 1938.

made on material which had been hydrolyzed by heating in a boiling water bath for six hours with two times normal sulfuric acid. Determinations for volatile acids and total hydrolyzable reducing substances were carried out on both feces and urine, while those for galacturonic acid and free reducing substances were made only on urine. Values for uronic acid in feces were obtained by the Link method,[17] which we have used in previous studies.[2c] By this method the recovery of pectin added to the feces is practically complete, as is the recovery of added galacturonic acid.

Galacturonic acid was estimated by the Kapp[18] method, reducing substances by the method of Hagedorn and Jensen[19] and the Somogyi modification[20] of the Shafer-Hartman method and volatile fatty acids by the Friedemann[21] method.

Absorption of Galacturonic Acid by the Ileum and Colon.—The galacturonic acid used was obtained, like the pectin, from the research department of the California Fruit Growers Exchange and is an enzymatic product of citrus pectin.[22] In analysis by the Link method[17] for determination of uronic acids, 21.8 per cent carbon dioxide, which is equivalent to 87.2 per cent uronic anhydride, was liberated. By the method of the Association of Official Agricultural Chemists for the determination of furfural,[23] 1 Gm. of the substance yielded 0.300 Gm. of phloroglucide.

Experiments were carried out on both human and canine subjects. Isolated loops of ileum (6 dogs) and colon (6 dogs) were studied in animals anesthetized with pentobarbital sodium. Three dogs with Thiery-Vella loops of the ileum and 1 dog with a similar loop of the colon were studied without anesthesia. Two human subjects with ileostomies were also studied without anesthesia. In all the experiments a 5 per cent solution of galacturonic acid having a Δ of -0.56 C. (isotonic and isosmotic with blood) and a p_H of 2.5 was used.

In the experiments with the anesthetized dogs the absorption period was two hours. For the unanesthetized dogs with loops of the ileum the absorption period was one hour, while for the dog with the loop of the colon it was two hours. In all of the experiments with dogs the loops were washed out with Ringer's solution before the galacturonic acid was introduced, and at the end of the absorption period the loop was drained and washed twice again, each time with 20 cc. of Ringer's solution. The latter washings were added to the fluid obtained from draining and marked for assay. The volume of the fluid drained and the final volume, after the washings were added, were noted.

The human subjects came to the laboratory in the morning without having had breakfast or drunk water. Since they had last eaten the evening before, the

17. Dickson, A. D.; Otterson, H., and Link, K. P.: The Determination of Uronic Acids, J. Am. Chem. Soc. **50**:775, 1930.

18. Kapp, E. M.: Microestimation of Uronic Acids, J. Biol. Chem. **134**:143, 1940.

19. Hagedorn, H. C., and Jensen, B. N.: Zur Mikrobestimmung des Blutzuckers mittels Ferricyanid, Biochem. Ztschr. **135**:46, 1923.

20. Somogyi, M.: A Method for the Preparation of Blood Filtrates for the Determination of Sugar, J. Biol. Chem. **86**:655, 1930.

21. Friedemann, T. E.: The Identification and Quantitative Determination of Volatile Alcohols and Acids, J. Biol. Chem. **123**:161, 1938.

22. Mottern, H. H., and Cole, H. L.: Enzymatic Preparation of d-Galacturonic Acid, J. Am. Chem. Soc. **61**:2701, 1939. Manville, I. A.; Reithel, F. J., and Yamada, P. M.: Note on the Preparation of d-Galacturonic Acid, ibid. **61**: 2973, 1939.

23. Official and Tentative Methods of Analysis, Association of Official Agricultural Chemists, ed. 4, Washington, D. C., The Association, 1935, p. 344.

bowel was practically empty, but a control test was performed first. They were given 200 cc. of distilled water to drink, and the value for the assay of the material in the ileostomy bags, obtained at the end of two hours, was subtracted from that for the assay carried out on material obtained at the end of a similar period after 200 cc. of the acid had been consumed.

All the assays included analyses by the previously mentioned methods of Link[17] and the Association of Official Agricultural Chemists.[23]

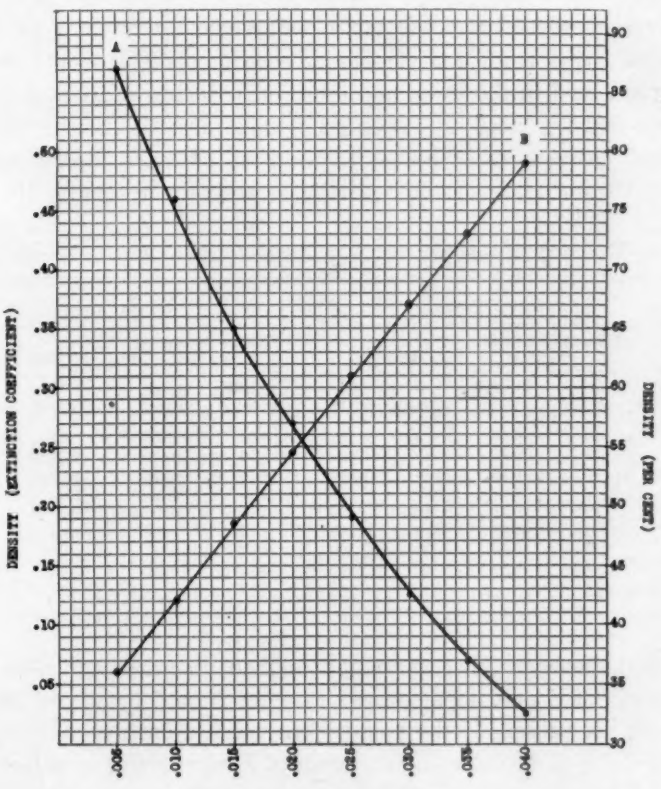

FIGURE 1.

Percentage (*A*) and extinction coefficient (*B*) curves for the recovery of galacturonic acid added to human urine.

RESULTS

Applicability of the Kapp Method for the Quantitative Recovery of Galacturonic Acid.—Since Kapp[18] did not include data about the quantitative recovery of pure galacturonic acid added to human urine, it was necessary for us to obtain such data and to test the method in our hands.

Normal human urine was assayed for galacturonic acid, and none was found. Pure galacturonic acid was added to the urine in quantities ranging from 5 to 40 micrograms for each 3.5 cc. An average recovery of 96.2 per cent of the added galacturonic acid was obtained. The averages of the data obtained in this work are given in table 1, and the corrected recovery curve is presented in the figure. (Kapp's article should be consulted for the details used in the calculations.)

Excretion of Galacturonic Acid and Reducing Substances in the Urine and Feces With and Without Pectin in the Diet.—The data on galacturonic acid in the urine and those on reducing substances in both the urine and the feces are recorded in table 2. No galacturonic acid was found in the urine of the subjects during either of the two absorption periods; no trace of color developed with the reagent. It should

TABLE 1.—*Recovery of Galacturonic Acid Added to Water and to Human Urine*

Galacturonic Acid Added to Water and Urine, Micrograms	Water				Human Urine			
	Stufenphotometer Reading		Recovery		Stufenphotometer Reading		Recovery	
	Percentage	Logarithm	Amount	Percentage	Percentage	Logarithm	Amount	Percentage
5	87	0.06	5	100	88.0	0.055	4.5	90.0
10	76	0.12	10	100	77.0	0.115	9.5	95.0
15	65	0.185	15	100	67.0	0.175	14.5	97.0
20	57	0.245	20	100	57.5	0.24	19.5	97.5
25	49	0.31	25	100	51.0	0.29	24.0	97.5
30	42.5	0.37	30	100	45.0	0.340	28.0	93.0
35	37	0.43	35	100	40.0	0.40	32.5	93.0
40	32.5	0.49	40	100	34.5	0.465	38.0	94.0
Average recovery.....				100				96.2

be recalled, however, that the Kapp method quantitatively determines galacturonic acid only in quantities ranging from 5 to 40 micrograms per 3.5 cc. of urine. If the twenty-four hour excretion of urine consisted of 1,200 cc. of urine and it contained 7 micrograms of galacturonic acid per 3.5 cc., to be measurable 2.4 mg. of galacturonic acid would need to be excreted. It should be added that the method employed is of such a nature that galacturonic acid is detected in the form of galacturonates. The total amount of reducing substances after hydrolysis while the subjects consumed the basal diet ranged from 380 to 1,240 mg. per hundred grams of feces and averaged 740 mg., while during the period that pectin was consumed the range was 220 to 930 mg. per hundred grams and the average was 770 mg.

The data show that as a result of the ingestion of 30 Gm. of pectin daily with a mixed diet no detectable increase in galacturonic acid and reducing substances in the urine occurred. This raises the question whether galacturonic acid is absorbed from the small intestine and the colon. This question will be considered later.

No significant difference was observed in the urinary excretion of free reducing substances. When calculated on the basis of 100 cc. samples and twenty-four hour volumes, the averages were 51.6 and 521 mg., respectively, during the period that the basal diet was consumed and 50 and 516 mg. during that in which pectin was consumed. The total amount of reducing substances in the urine after hydrolysis averaged

TABLE 2.—*Excretion of Galacturonic Acid and Reducing Substances in the Urine and Feces of Subjects Consuming the Basal Diet With and Without the Addition of Pectin*

		Urine							Feces,
				Free Reducing Substances		Total of Reducing Substances After Hydrolysis			
Subject	Specimen Designation	Volume of 24 Hour Specimen, Cc.	Galacturonic Acid in 24 Hour Specimen, Mg.	Mg. per 100 Cc.	Mg. in 24 Hour Specimen	Mg. per 100 Cc.	Mg. in 24 Hour Specimen	Hydrolyzable Reducing Substances in 24 Hour Specimen, Mg.	Total of Reducing Substances After Hydrolysis, Mg. per 100 Gm.
				Basal Diet					
1	a	1,340	0	..	...	382	5,119	.....	380
	b	1,500	0	..	...	...	.....	.....	570
2	a	1,190	0	..	...	274	3,261	.....	1,240
	b	1,170	0	..	...	253	2,960	.....	750
3	a	1,200	0	46	557	336	4,066	3,509	580
	b	1,130	0	49	553	282	3,187	2,634	780
4	a	980	0	51	500	292	2,862	2,362	820
	b	870	0	56	495	256	2,217	1,722	740
5	a	1,120	0	44	493	264	2,957	2,464	680
	b	1,080	0	46	497	282	3,046	2,549	720
6	a	900	0	58	522	336	3,024	2,502	820
	b	880	0	63	554	340	2,992	2,438	780
Average.....			0	51.6	521	300	3,245	2,522	740
				Pectin and Basal Diet					
1	a	1,273	0	..	...	361	4,596	.....	750
	b	1,254	0	..	...	350	4,389	.....	930
2	a	1,023	0	..	...	376	3,846	.....	680
	b	1,080	0	..	...	333	3,596	.....	220
3	a	1,360	0	41	558	308	4,189	3,631	650
	b	1,200	0	49	588	318	3,716	3,128	680
4	a	950	0	53	504	242	3,000	2,500	760
	b	800	0	61	488	292	2,336	1,848	720
5	a	1,220	0	41	500	238	2,904	2,404	650
	b	980	0	49	480	300	2,940	2,460	720
6	a	910	0	56	510	326	2,967	2,457	840
	b	940	0	53	498	318	2,989	2,491	880
Average.....			0	50.0	516	313	3,456	2,615	770

300 mg. per hundred cubic centimeters and 3,245 mg. per twenty-four hour volume while the subjects were on the basal diet and 313 mg. per hundred cubic centimeters and 3,456 mg. per twenty-four hour specimen while they consumed the pectin-containing diet. The amount of hydrolyzable reducing substances, on the basis of twenty-four hour excretion, was calculated by subtracting the value for free reducing substances from that for the total amount of reducing substances after hydrolysis. The

average value while the basal diet was consumed was 2,522 mg. and that for the period when the pectin-containing diet was used was 2,615 mg.

Excretion of Volatile Acids in the Urine With and Without Pectin in the Diet.—Table 3 provides the data on the excretion of volatile acids in the urine with and without pectin in the diet. The values for formic acid, in terms of cubic centimeters of tenth normal alkali per twenty-four

TABLE 3.—*Excretion of Volatile Acids in the Urine of Subjects Consuming the Basal Diet With and Without the Addition of Pectin*

Subject	Specimen Designation	Volume of 24 Hour Specimen, Cc.	First Distillation, Cc. of N/100 Alkali		Second Distillation, Cc. of N/100 Alkali		Formic Acid,* Cc. of N/10 Alkali per 24 Hour Specimen	Acetic Acid, Cc. of N/10 Alkali per 24 Hour Specimen
			Per 100 Cc.	Per 24 Hour Specimen	Per 100 Cc.	Per 24 Hour Specimen		
Basal Diet								
1	a	1,340	71.2	954	39.6	531	42	53
	b	1,500	56.8	852	51.2	765	8	77
2	a	1,190	93.4	1,111	68.6	821	29	82
	b	1,170	32.6	381	26.0	294	9	29
3	a	1,210	29.8	361	16.6	206	15	21
	b	1,130	45.6	515	27.6	316	20	32
4	a	980	26.4	259	17.2	167	9	17
	b	870	42.8	372	21.2	183	19	18
5	a	1,120	41.6	466	35.2	394	7	39
	b	1,080	54.0	583	44.8	483	10	48
6	a	900	50.8	459	40.0	360	10	36
	b	880	61.6	546	54.0	475	7	48
Average			50.5	572	36.8	416	15	42
Pectin and Basic Diet								
1	a	1,273	51.0	649	42.7	547	10	55
	b	1,254	60.3	752	55.4	690	6	69
2	a	1,023	74.8	767	65.2	665	10	67
	b	1,080	93.4	1,007	55.0	594	41	59
3	a	1,360	28.0	381	20.0	272	11	27
	b	1,200	40.0	480	31.4	372	11	37
4	a	950	35.2	333	23.2	219	11	22
	b	800	36.4	288	22.4	176	11	18
5	a	1,220	54.8	669	48.8	594	7	59
	b	980	59.6	584	48.8	478	8	49
6	a	910	64.8	590	59.6	542	5	54
	b	940	61.2	575	52.0	489	9	49
Average			55.0	590	43.7	470	12	47

* The values for formic acid are not absolute, since the analytic method used does not exclude all of any pyruvic acid which may be present.

hour specimen, were obtained by subtracting the results on the second distillation from those of the first distillation. The value for acetic acid is also indicated in terms of cubic centimeters of tenth normal alkali per twenty-four hour specimen. The values obtained from the second distillation were used. The average values for the excretion of formic acid and acetic acid in the samples from the 6 subjects while they were on the basal diet were 15 and 42 cc., respectively, while average values of 12 and 47 cc. were recorded for the period during which they consumed the test diet containing pectin.

It should be pointed out that the values for formic acid are not absolute since the analytic method used does not exclude all of any pyruvic acid which may be present.[21]

The results show that the presence of pectin in the diet does not significantly increase the excretion of formic and acetic acids in the urine.

Excretion of Volatile Acids in the Feces With and Without Pectin in the Diet.—The values obtained for the excretion of volatile acids in the feces before and after pectin was added to it are shown in table 4. The results for the excretion of formic and acetic acids presented in this table were calculated in the manner previously indicated for the excretion

TABLE 4.—*Excretion of Volatile Acids in the Feces of Subjects Consuming the Basal Diet With and Without the Addition of Pectin*

Subject	Specimen Designation	First Distillation, Cc. of N/100 Alkali per 100 Gm.		Second Distillation, Cc. of N/100 Alkali Per 100 Gm.		Formic Acid,* Cc. of N/10 Alkali per 100 Gm.		Acetic Acid, Cc. of N/10 Alkali per 100 Gm.	
		Basal Diet	Pectin and Basal Diet	Basal Diet	Pectin and Basal Diet	Basal Diet	Pectin and Basal Diet	Basal Diet	Pectin and Basal Diet
1	a	1,920	1,920	1,840	1,800	8	12	184	180
	b	2,040	1,520	1,920	1,400	12	12	192	140
2	a	1,320	1,520	1,240	1,440	8	8	124	144
	b	1,240	1,560	1,160	1,400	8	16	116	140
3	a	1,200	880	1,160	840	4	4	116	84
	b	720	1,240	600	1,200	12	4	60	120
4	a	1,260	1,800	1,200	1,720	6	8	120	172
	b	960	1,680	920	1,560	4	12	92	156
5	a	1,024	900	992	836	3	6	99	84
	b	896	984	832	920	6	6	83	84
6	a	952	992	892	908	6	8	89	91
	b	1,020	1,048	956	992	6	6	96	99
Average.....		1,213	1,505	1,164	1,251	7	8.5	114	127

* The values for formic acid are not absolute, since the analytic method used does not exclude all of any pyruvic acid which may be present.

of these substances in the urine, but they are given in terms of cubic centimeters of tenth normal alkali per hundred grams of feces. For the periods in which the basal diet and the pectin-containing diet were consumed, the average excretion of formic acid were 7 and 8.5 cc. of tenth normal alkali, respectively, and for the excretion of acetic acid the values were 114 and 127 cc.

These results indicate a tendency toward an increase in the excretion of volatile acids in the feces after pectin is ingested, but the tendency is not sufficiently pronounced to be definitely significant. It should be explained that these results hold only for the addition of pectin to a mixed diet and do not necessarily apply to the administration of pectin alone or to the effect of administration of pectin in the presence of diarrhea or in the absence of protein from the diet, conditions which affect the flora of the colon.

Absorption of Galacturonic Acid from the Small Intestine and the Colon.—If galacturonic acid is absorbed from the small or the large intestine it should appear in the urine as a galacturonate, unless it is oxidized in the tissues. Our failure to find measurable quantities of galacturonic acid in the urine caused us to ascertain whether it is absorbed.

The recovery of galacturonic acid from the ileum and that from the colon after a two hour absorption period in the case of the anesthetized animals were practically the same (table 5). Recovery from the ileum was 93 per cent by both the phloroglucide and the uronic acid method, while recovery from the colon was 91 per cent by the phloroglucide method and 94 per cent by the uronic acid method. In these experiments

TABLE 5.—*Recovery of Galacturonic Acid from the Ileums and from the Colons of Anesthetized Dogs*

Experiment	Loop	Volume of Fluid Introduced, Cc.	Volume of Fluid Drained, Cc.	Final Volume, Cc.	Recovery of Galacturonic Acid			
					By Phloroglucide Method		By Uronic Acid Method	
					Grams	Percentage	Grams	Percentage
1	Ileum	50	56	95	0.665	88	0.505	92
2	Ileum	50	46	82	0.695	93	0.515	95
3	Ileum	50	52	90	0.720	96	0.515	94
4	Ileum	50	60	96	0.700	93	0.510	93
5	Ileum	50	52	90	0.675	90	0.495	91
6	Ileum	50	56	92	0.700	93	0.525	96
Average					0.692	93	0.511	93
1	Colon	50	48	84	0.705	94	0.520	96
2	Colon	50	46	80	0.690	92	0.530	97
3	Colon	50	48	82	0.665	88	0.490	90
4	Colon	50	50	90	0.665	89	0.510	94
5	Colon	50	50	86	0.670	89	0.490	90
6	Colon	50	46	80	0.710	95	0.520	95
Average					0.684	91	0.510	94

the volume of fluid drained at the end of the test period was practically the same as that which was introduced. Recovery of galacturonic acid from the ileum and that from the colon in the case of the unanesthetized dogs with Thiery-Vella loops were also much the same (table 6). Recovery from the ileum was 90 per cent by the phloroglucide method and 94 per cent by the uronic acid method. The volume of fluid drained from the ileum in these experiments was greater in every instance than that introduced, while the volume of fluid drained from the colon was smaller than that introduced.

From the loops of human subjects who had undergone ileostomy the average recovery of galacturonic acid was 91 per cent by the phloroglucide method and 95 per cent by the uronic acid method. The volumes of fluid in the ileostomy bags obtained in all of the control experiments

were less than those obtained in all of the test experiments. The control volumes (table 7) for experiments 1a and 1b were 50 and 60 cc., respectively, while for experiments 2a and 2b they were 85 and 140 cc., respectively.

TABLE 6.—*Recovery of Galacturonic Acid from the Ileums of Three Unanesthetized Dogs and from the Colon of One*

Dog	Experiment	Location of Thiery-Vella Loop	Volume of Fluid Introduced, Cc.	Volume of Fluid Drained, Cc.	Final Volume, Cc.	Recovery of Galacturonic Acid: By Phloroglucide Method, Grams	By Phloroglucide Method, Percentage	By Uronic Acid Method, Grams	By Uronic Acid Method, Percentage
1	a	Ileum	25	35	70	0.315	84	0.250	92
	b	Ileum	25	40	75	0.340	90	0.265	96
	c	Ileum	25	32	70	0.350	93	0.260	95
Average						0.335	90	0.258	95
2	a	Ileum	50	65	100	0.650	87	0.520	96
	b	Ileum	50	60	95	0.665	89	0.520	96
	c	Ileum	50	58	95	0.665	89	0.500	92
Average						0.660	88	0.513	95
3	a	Ileum	40	50	88	0.530	88	0.405	93
	b	Ileum	40	55	90	0.540	90	0.425	97
	c	Ileum	40	60	100	0.550	92	0.410	94
Average						0.540	90	0.410	94
Average for the 3 dogs						.....	89	.....	94
1	a	Colon	50	30	65	0.650	86	0.485	89
	b	Colon	50	35	70	0.665	89	0.505	93
	c	Colon	50	25	60	0.690	92	0.515	95
	d	Colon	50	30	70	0.630	84	0.490	90
	e	Colon	50	30	65	0.620	82	0.470	86
	f	Colon	50	40	80	0.680	91	0.530	97
Average						0.656	87	0.500	92

TABLE 7.—*Recovery of Galacturonic Acid from Human Subjects Who Had Undergone Ileostomy*

Subject	Experiment	Volume of Fluid Given, Cc.	Volume of Fluid Recovered, Cc.	Recovery of Galacturonic Acid: By Phloroglucide Method, Grams	By Phloroglucide Method, Percentage	By Uronic Acid Method, Grams	By Uronic Acid Method, Percentage
1	a	200	340	2.85	95	2.05	95
	b	200	410	2.75	91	2.10	95
2	a	200	360	2.65	89	2.00	92
	b	200	600	2.80	94	2.10	96
Average				2.76	91	2.06	95

Since in all of the experiments the average values for recovery were practically 90 per cent or more and since the difference between these values and 100 per cent recovery may be accounted for by the errors inherent in the methods employed, we concluded that if galacturonic acid was absorbed at all, the amount was very small.

COMMENT

The results show that the addition of 30 Gm. of pectin to a mixed diet did not significantly increase the fecal and urinary excretion of volatile acids, particularly formic and acetic acids. Such volatile acids as are produced during the decomposition of pectin in the colon are to a large extent oxidized either in the colon or in the tissues. Our data on the excretion of volatile acids in the urine confirm the unpublished data of Dr. T. E. Friedemann, whose method we used. He observed, as did we, that the excretion of acetic acid varies considerably in different subjects, while the excretion of formic acid is more constant.

The formation of methyl alcohol from pectin in the colon is possible. If methyl alcohol is found in appreciable quantities, most of it must be exhaled or otherwise disposed of, since appreciable increase in the excretion of formic acid in the urine was not observed when we administered pure citrus pectin. Voit and Friedrich [14] fed a pectin preparation called aplona and observed a slight increase in the excretion of formic acid in the urine. Apparently, they performed only 1 experiment on 1 subject, and when our values for the excretion of formic acid are converted into milligrams and compared with their results, the small increase observed by them falls within the range of daily variation observed for our subjects. The difference in results, however, may be due to the difference in the product used.

Our resuts show that galacturonic acid is not absorbed in significant amounts from the small intestine of the canine or the human subject or from the colon of the dog. This fact and our failure to find galacturonic acid in the urine in the presence of pectin in the diet shows that pectin, by providing galacturonic acid, cannot favor the detoxicatory function of the liver, by which certain phenolic compounds are known to be conjugated with glucuronic acid. Malyoth [1b] stated, without giving data or methods, that a high percentage of galacturonic acid given to animals can be recovered in the feces and that galacturonic acid given parenterally is found unconjugated in the urine.

Our results, as well as those of Kertesz, Walker and McCoy,[24] strongly indicate that one must study the local effects of apple and pectin in the alimentary tract to discover how their favorable effect on diarrhea is exerted. The cellulose and lignin in apples probably act as absorbing colloids, or mechanically, since they are not appreciably decomposed. Pectin, which is decomposed only in the colon, could act similarly in the small intestine but not in the colon, unless, as in the fasting dog, a considerable amount of the pectin is not decomposed. It is possible that the decomposition of pectin produces an unfavorable

24. Kertesz, Z. I.; Walker, M. S., and McCoy, C. M.: The Effect of Feeding Apple Sauce on Induced Diarrhea in Rats, Am. J. Digest. Dis. **8**:124, 1941.

medium for the organisms causing diarrhea. The offending organisms may actually be destroyed by the acids produced, or when the diet of the patient is chiefly apple or pectin, they may be starved out or be overgrown by organisms which use pectin as a source of food.

CONCLUSIONS

The decomposition of citrus pectin in the colon in young men on a mixed diet does not significantly change the excretion of formic acid, acetic acid, which are volatile acids, and reducing substances in the urine and the feces.

Pectin is not excreted in the urine as galacturonates in quantities which can be measured by the micromethod of Kapp.

Galacturonic acid is not absorbed in appreciable quantities from the human and canine small intestine and colon. Hence, the favorable effects of a diet containing apple or pectin in the treatment of diarrhea cannot be ascribed to an improvement of the detoxicatory function of the liver as a result of the absorption of galacturonic acid. The favorable effects, according to our evidence, are exerted exogenously in the lumen of the bowel.

DOMESTIC WATER AND DENTAL CARIES

III. FLUORINE IN HUMAN SALIVA

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The presence of 0.095 part of fluorine per million in a pooled sample of saliva collected from 3 girls aged 8 living in Galesburg, Ill., and 0.120 part per million in a pooled specimen collected from 3 girls of the same age living in Quincy, Ill., has been reported by Cox.[1] More recently, Wills [2] reported that radioactive fluorine administered intravenously to a cat appeared within one minute in the saliva of the submaxillary glands. Boissevain and Drea,[3] however, found no fluoride in human saliva collected in an area where mottled enamel was prevalent.

The specimens of saliva for which data are given in table 1 were collected by paraffin stimulation and represent continuous secretions of approximately 100 cc. of saliva. The samples reported on in table 2 were pooled specimens collected from groups of white public school children, comprising from 40 to 200 persons per group, who were the subjects of epidemiologic studies of dental caries.[4] The specimens of saliva in this case were collected by paraffin stimulation, but only 10 to 15 cc. was collected from each subject, part of which went into the pooled sample for analysis. All samples were preserved with thymol and were placed in the cold as soon as possible after collection.

Analysis for fluorine was made on a 100 cc. sample of saliva, which was placed in a platinum evaporating dish, made alkaline with dilute sodium hydroxide and evaporated to dryness on a water bath. Five

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From the Division of Infectious Diseases, National Institute of Health, the United States Public Health Service, in cooperation with the Division of Chemistry.

Dental Surgeon H. T. Dean and Passed Assistant Dental Surgeon Francis A. Arnold Jr., of the Division of Infectious Diseases, National Institute of Health, cooperated in collecting samples of saliva outside the area of Washington, D. C., and Senior Chemist Elias Elvove, of the Division of Chemistry, National Institute of Health, furnished data relative to the fluoride content of city water supplies.

1. Cox, G. J.: J. Am. Dent. A. **27**:1107, 1940.

2. Wills, J. H.: J. Dent. Research **19**:585, 1940.

3. Boissevain, C. H., and Drea, W. F.: J. Dent. Research **13**:495, 1933.

4. (*a*) Dean, H. T.; Jay, P.; Arnold, F. A., Jr.; McClure, F. J., and Elvove, E.: Pub. Health Rep. **54**:862, 1939. (*b*) Dean, H. T.; Jay, P.; Arnold, F. A., Jr., and Elvove, E.: ibid. **56**:365, 1941. (*c*) Arnold, F. A., Jr., and McClure, F. J.: ibid., to be published. (*d*) Dean, H. T.; Jay, P.; Arnold, F. A., Jr., and Elvove, E.: ibid. **56**:761, 1941.

TABLE 1.—*Fluorine Content of Saliva*

Samples* from adults		Location	Fluorine in Drinking Water, Parts per Million	Fluorine in Saliva, Parts per Million
F. J. Mc.	1939	Washington, D. S.	0.0†	<0.10‡ (0.04-0.09)
F. J. Mc.	1940	Washington, D. C.	0.0	0.10
C. C.	1939	Washington, D. C.	0.0	0.12
A. K.	1939	Washington, D. C.	0.0	0.12
W. T. H.	1939	Washington, D. C.	0.0	0.14
H. D.	1939	Washington, D. C.	0.0	0.12
E. E.	1939	Washington, D. C.	0.0	0.12
C. M.	1940	College Park, Md.	...	<0.10 (0.05)
A. H.	1940	Baltimore	...	<0.10 (0.07)
W. H.	1940	Washington, D. C.	0.0†	<0.10 (0.08)
Samples* from children				
No. 1	1938	Amarillo, Texas§	3.8-4.0	0.19
No. 2	1938	Amarillo, Texas	3.8-4.0	0.17
No. 3	1938	Amarillo, Texas	3.8-4.0	0.19
No. 4	1938	Amarillo, Texas	3.8-4.0	0.18
No. 5	1938	Amarillo, Texas	3.8-4.0	0.24
No. 6	1938	Amarillo, Texas	3.8-4.0	0.17
No. 7	1938	Amarillo, Texas	3.8-4.0	0.20
No. 8	1938	Amarillo, Texas	3.8-4.0	0.15
No. 9	1938	Amarillo, Texas	3.8-4.0	0.14
No. 10	1938	Amarillo, Texas	3.8-4.0	0.16
No. 11	1938	Amarillo, Texas	3.8-4.0	0.13

* The individual specimens were of 100 cc. each.

† One test made on this water showed a negative fluorine content, that is, not more than 0.10 parts per million.

‡ Average fluorine content of 10 100 cc. specimens.

§ Collected in January 1938, during a study of dental caries conducted by the Division of Infectious Diseases and Child Hygiene Section, Division of Public Health Methods.

TABLE 2.—*Fluorine Content of Pooled Specimens of Children's Saliva*

Location	Year	Fluorine in Drinking, Water, Parts per Million	Fluorine in Saliva, Parts per Million	No. of Specimens Pooled	Comment*
Galesburg, Ill.	1938	1.8	0.16	82	Specimens obtained from 12, 13 and 14 year old children
Quincy, Ill.	1938	0.2	0.14	63	Specimens obtained from 12 to 14 year old children
Arlington, Va., October	1939	0.0	0.10	128	Specimens obtained in three different months were from the same 12 to 14 year old children
Arlington, Va., December	1939	0.0	<0.10 (0.06)	116	
Arlington, Va., March	1940	0.0	<0.10 (0.07)	126	
Elmhurst, Ill.	1940	1.8	0.16	150	Specimens obtained from 12 to 14 year old school children
Joliet, Ill.	1940	1.3	0.10	200	Specimens obtained from 12 to 14 year old school children
Maywood, Ill.	1940	1.2	0.10	125	Specimens obtained from 12 to 14 year old school children
Aurora, Ill.	1940	1.2	0.10	75	Specimens obtained from 12 to 14 year old school children
Evanston, Ill.	1940	0.0	<0.10 (0.08)	200	Specimens obtained from 12 to 14 year old school children
Oak Park, Ill.	1940	0.0	<0.10 (0.07)	150	Specimens obtained from 12 to 14 year old school children
Bauxite, Ark.†	1940	0.0	0.15	50	Specimens obtained from 14 to 22 year old subjects with mottled enamel
Bauxite, Ark.	1940	0.0	0.10	49	Specimens obtained from 8 to 13 year old subjects not having mottled enamel
Benton, Ark.	1940	0.0	<0.10 (0.06)	41	Specimens obtained from 14 to 21 year old subjects not having mottled enamel
Garrettsville, Ohio	1940	0.7	0.11	80	Specimens collected from the same 9 to 14 year old children on succeeding days
Garrettsville, Ohio	1940	0.7	0.13	80	

* All of the children were white.

† The public water supply of Bauxite prior to 1928 contained about 14 parts of fluorine per million.

cubic centimeters of 5 per cent magnesium acetate was added and the sample dried and ashed at 500 C. The fluorine content was determined on the ash by distillation from perchloric acid and titration with standard thorium nitrate. Further details of the method are contained in an article by McClure.[5] The percentage recoveries of 0.10 part of fluorine per million, which was added to 3 samples of saliva collected in Garretsville, Ohio, equaled 85, 95 and 82. If a 100 cc. sample of saliva is used for analysis the method is considered only approximate for quantities of fluorine of the order of 0.10 part per million or less. By the same procedure, 3 samples of cow's milk obtained from a local dairy were found to contain 0.16, 0.13 and 0.14 part of fluorine per million respectively. These results are similar to those reported by Phillips and Hart.[6]

The data shown in table 1 indicate that the fluorine content of the saliva of normal adults (specimens obtained in Washington, D. C., and vicinity) averages about 0.10 part per million. The specimens of saliva obtained from school children of Amarillo, Texas (where there were 3.8 to 4.0 parts of fluorine per million in the drinking water) showed a fluorine content slightly above 0.10 part per million. If one considers the results of analysis of pooled specimens of saliva (table 2) collected in various cities in which the drinking water varied in fluorine content from 0.0 to 1.8 parts per million, the data cannot be said to show a consistent effect of the level of fluorine in the drinking water on the fluorine content of human saliva.[7] The results presented in table 2, like those in table 1, indicate that the quantity of fluorine in normal saliva is equal to about 0.10 part per million.

It is to be noted in this connection that according to the data presented by Dean and co-workers,[4d] the Illinois cities of Elmhurst, Joliet, Maywood, Aurora, Evanston and Oak Park showed pronounced differences in their dental caries experience rate. According to the results for the fluorine content of the saliva of subjects representing these respective cities (table 2), an increased amount of fluorine in the saliva is not responsible for the observed differences in the caries rates of these cities. Likewise, similar quantities of fluorine were found in specimens of saliva collected at Galesburg and at Quincy, Ill., in 1938. (Data reported by Cox [1] also indicated that there were similar quantities of fluorine in the saliva of subjects from these two cities.) The caries rate for Galesburg, however, was 201 per hundred children and for Quincy 633 per hundred children.[4a]

5. McClure, F. J.: Indust. & Engin. Chem. (Analyt. Ed.) **18**:171, 1939.

6. Phillips, P. H., and Hart, E. B.: J. Biol. Chem. **105**:123, 1934.

7. The sensitivity of the method does not permit any significance to be attached to differences of 0.05 parts per million or less between the analytic results for fluorine.

No conclusions appear to be justified at this time with regard to the significance of the quantity of fluorine which is normally present in saliva. Any function which this normal quantity or any slight excess above normal may have as a partial preventive of dental caries [8] remains to be demonstrated. More data are needed, also, to establish any relation between the fluorine content of the drinking water and the resulting excretion of fluorine in the saliva.

8. Dean, Jay, Arnold, McClure and Elvove,[4a] Dean, Jay, Arnold and Elvove (footnotes 4 *b* and 4 *d*).

EFFECT OF ADDING VITAMIN B COMPLEX TO THE DIETS OF STABILIZED DIABETIC CHILDREN

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The close relation between thiamine and carbohydrate metabolism is well established. In uncomplicated diabetes mellitus the evidence for the value of therapeutic doses of vitamin B complex is confusing. Trasoff and Bordin [1] reviewed the literature and reported their experience with administering thiamine hydrochloride to 15 diabetic patients. They observed no significant improvement in the patients studied which they could attribute to the thiamine therapy. They pointed out that "in a clinical investigation of this nature where the laboratory reports occupy such an important place and where there is a likelihood of variations due to many factors, one must be careful in accepting a blood-sugar lowering 10-20 per cent or thereabouts as positive proof of the beneficent effect of Vitamin B_1. Over-enthusiasm may lead to erroneous conclusions." Smith and Mason [2] reported no change in the insulin requirement of diabetic subjects following thiamine deprivation and therapy.

In former publications [3] from this department the need for standardized and well established control of diabetes mellitus in the child has been emphasized, not only for the management of the disease but as a prerequisite for studies concerned with the relative efficacy of various forms of treatment.

The constancy of response which may be attained with the therapeutic regimen used for children is illustrated in chart 1.[3a] This chart shows the mean blood sugar levels and the diurnal blood sugar fluctuations of

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From the Department of Pediatrics, State University of Iowa College of Medicine.

1. Trasoff, A., and Bordin, C.: The Use of Vitamin B_1 in Diabetes Mellitus: A Clinical Study, Am. J. Digest. Dis. **8**:1-34 (Jan.) 1941.

2. Smith, K. A., and Mason, H. L.: Thiamin and Diabetes Mellitus, Proc. Staff Meet., Mayo Clin. **15**:529-532 (Aug. 21) 1940.

3. (*a*) Jackson, R. L.; Boyd, J. D., and Smith, T. E.: Interchangeability of Zinc Crystalline Insulin and Amorphous Insulin, Am. J. Dis. Child. **59**:1050-1053 (May) 1940; (*b*) Stabilization of the Diabetic Child, ibid. **59**:332-341 (Feb.) 1940.

31 stabilized diabetic patients, as contrasted with the range observed for nondiabetic children. The values in chart 1 show the degree of oscillation and the type of blood sugar level encountered in observations on 31 stabilized subjects. The data, which include an aggregate of 906 blood sugar estimations made during six hundred and eleven days of study, prove the practicability of maintaining approximately normal blood sugar levels in the diabetic child.

In previous publications [8] data were presented to indicate the fallacy of conclusions regarding the apparent insulin requirement of diabetic subjects who had not reached full stability before the studies were under-

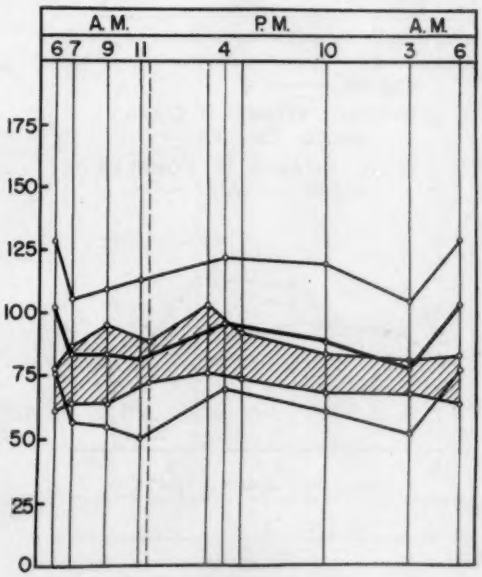

Chart 1.—Diurnal blood sugar fluctuation of normal children as contrasted with that of well stabilized diabetic children. The cross-hatched area represents the gross range of the values obtained for nondiabetic children; the heavy line represents the average values, and the other two curves bound the range included by two standard deviations of the values for children with diabetes mellitus. Each group was under the same dietary regimen; the children with diabetes received insulin.

taken. Unless investigators can offer evidence of preliminary constancy of insulin dosage for some time in conjunction with a strictly defined regimen and freedom from glycosuria, conclusions drawn from such data can be seriously questioned. It has been shown that if patients continue with their hospital regimen and the insulin dosage is kept at a level which avoids both glycosuria and severe insulin shock the insulin requirement decreases rapidly until a lower, stable level is reached.

The study on which this report is based was undertaken to determine if the addition of vitamin B complex to our standard diets for diabetic patients would alter the patient's insulin requirement. The subjects used for study were 5 diabetic children whose status satisfied the following criteria: (1) prolonged preliminary observation, during which the insulin requirement had become constant and adequate for the standard conditions imposed by the therapeutic regimen; (2) maintained aglycosuria and freedom from clinically significant insulin shock, and (3) approximately normal diurnal blood sugar fluctuations from day to day.

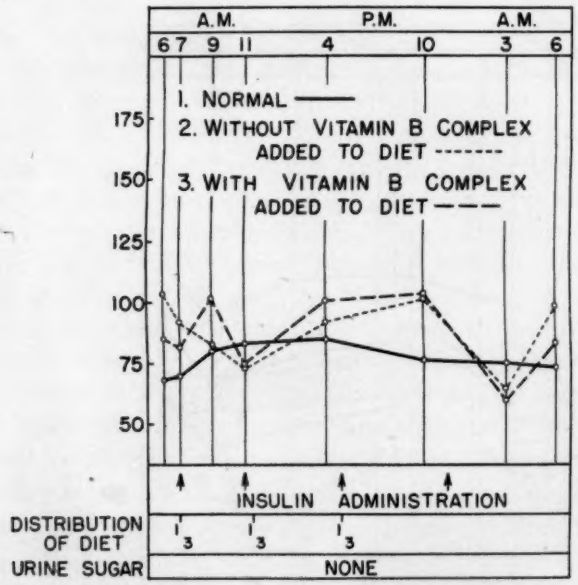

Chart 2.—Average diurnal blood sugar fluctuations of well stabilized diabetic children given a standard diet with and without the addition of vitamin B complex, other factors being constant. In each instance the regimen and the response had been constant for several days before the blood sugar values were accepted for inclusion (the figures were based on an aggregate of 306 determinations of blood sugar made during one hundred and twenty-six hospital days). The heavy line in the chart indicates the average blood sugar values obtained in observations on nondiabetic children under a similar dietary regimen (chart 1).

Blood sugar determinations were made serially on one or more days each week at the following hours: 6 a. m., 7 a. m., 9 a. m., 11 a. m., 4 p. m., 10 p. m., 3 a.m. and 6 a. m. A micromodification of the Folin-Wu method was used for estimation of sugar content; the Somogyi method of precipitation was employed. Insulin was administered at 6:30 a. m., 11 a.m. and 4:30 p. m. and once during the night (at 10,

Thiamine Content of Standard Diets for Diabetic Subjects *

Day's Diet	Protein 50 Gm. Carbohydrate 100 Gm. Fat 75 Gm.		Protein 55 Gm. Carbohydrate 110 Gm. Fat 82 Gm.		Protein 60 Gm. Carbohydrate 120 Gm. Fat 90 Gm.		Protein 65 Gm. Carbohydrate 130 Gm. Fat 98 Gm.		Protein 70 Gm. Carbohydrate 140 Gm. Fat 105 Gm.		Protein 75 Gm. Carbohydrate 150 Gm. Fat 113 Gm.		Protein 80 Gm. Carbohydrate 160 Gm. Fat 12 Gm.	
	Weight, Gm.	Thiamine, Micrograms	Weight, Gm.	Thiamine, Micrograms	Weight, Gm.	Thiamine, Micrograms	Weight, Gm.	Thiamine, Micrograms	Weight, Gm.	Thiamine, Micrograms	Weight, Gm.	Thiamine, Micrograms	Weight, Gm.	Thiamine, Micrograms
Orange	75	57	75	57	75	57	75	57	75	57	75	57	75	57
Oatmeal	12	105	12	105	12	105	15	131	15	131	18	157	18	157
Eggs	50	44	60	53	100	88	110	97	120	106	145	84	170	150
Bread, white	10	..	25	..	35	..	45	..	55	..	55	..	65	..
Butter	34	..	41	..	45	..	50	..	58	..	65	..	70	..
Milk	960	375	960	375	960	375	960	375	960	375	960	375	960	375
Beef	30	57	40	76	30	57	40	76	45	85	50	95	55	105
Potato	50	58	45	50	75	83	90	99	120	132	160	176	180	198
Tomatoes	100	52	100	52	100	52	100	52	100	52	100	52	100	52
Apple	100	28	100	28	100	28	100	28	100	28	100	28	100	28
Peas	65	260	65	260	65	260	65	260	65	260	65	260	65	260
Grapefruit	70	35	70	35	70	35	70	35	70	35	70	35	70	35
Total thiamine content		1,071		1,091		1,140		1,210		1,261		1,319		1,417
Total thiamine content		1.07 mg.		1.09 mg.		1.14 mg.		1.21 mg.		1.26 mg.		1.32 mg.		1.42 mg.

Day's Diet	Protein 63 Gm. Carbohydrate 135 Gm. Fat 99 Gm.		Protein 70 Gm. Carbohydrate 150 Gm. Fat 110 Gm.		Protein 77 Gm. Carbohydrate 165 Gm. Fat 121 Gm.		Protein 84 Gm. Carbohydrate 180 Gm. Fat 132 Gm.		Protein 91 Gm. Carbohydrate 195 Gm. Fat 143 Gm.		Protein 98 Gm. Carbohydrate 210 Gm. Fat 154 Gm.		Protein 105 Gm. Carbohydrate 225 Gm. Fat 165 Gm.	
	Weight, Gm.	Thiamine, Micrograms	Weight, Gm.	Thiamine, Micrograms	Weight, Gm.	Thiamine, Micrograms	Weight, Gm.	Thiamine, Micrograms	Weight, Gm.	Thiamine, Micrograms	Weight, Gm.	Thiamine, Micrograms	Weight, Gm.	Thiamine, Micrograms
Orange	75	57	75	57	75	57	75	57	112	85	112	85	112	85
Oatmeal	20	175	20	175	24	209	26	226	26	226	26	226	26	226
Eggs	100	88	130	114	150	132	170	150	190	167	220	194	240	211
Bread, white	45	..	60	..	60	..	75	..	85	..	110	..	140	..
Butter	54	..	64	..	73	..	81	..	94	..	101	..	106	..
Milk	960	375	960	375	960	375	960	375	960	375	960	375	960	375
Beef	35	66	40	76	50	95	60	113	70	133	80	152	90	170
Potato	100	116	130	150	200	232	200	232	200	232	200	232	200	232
Tomato	100	52	100	52	100	52	100	52	100	52	100	52	100	52
Apple	100	28	100	28	100	28	100	28	150	42	150	42	150	42
Peas	65	260	65	260	65	260	65	260	85	340	85	340	85	340
Grapefruit	70	35	70	35	70	35	70	35	100	51	100	51	100	51
Total thiamine content		1,252		1,322		1,475		1,528		1,703		1,749		1,784
Total thiamine content		1.3 mg.		1.3 mg.		1.5 mg.		1.5 mg.		1.7 mg.		1.7 mg.		1.8 mg.

* Data on the thiamine content of the foods listed were obtained from the National Livestock and Meat Board, Chicago. The diets are contained in "Diabetic Diets for Children" (in Daum, K.: Diets, ed. 2, Iowa City, Williams Surgical Supply Co., 1939, pp. 63-65). The thiamine content of the diets was calculated by Catherine Smith, M.S., of the nutrition department of the University Hospitals, State University of Iowa.

12 or 2 o'clock). The total day's dose was distributed among the four injections, with a percentage distribution ratio of approximately 35, 22, 28 and 15.

Each of the 5 stabilized children with diabetes mellitus who were used as subjects for this special study had been in the hospital, under exacting management, for several weeks and had had normal blood sugar levels and constancy of insulin dosage for periods averaging one week. The constancy of the diabetic status was further evidenced by the course of the subjects during the periods of special study, which averaged twenty-five days. During the special study the control regimen was altered in one respect only: thiamine (2 to 3 mg.) in the form of vitamin B complex, was added to the diet daily. The average blood sugar levels observed when the children were receiving the standard diets of diabetic subjects and the standard diets with the addition of vitamin B complex are shown graphically in chart 2. Two of the patients were observed for another period, which averaged two weeks, during which vitamin B complex was no longer added to their diets. No change was noted in their response. The results are interpreted as evidence that the ingestion of vitamin B complex in excess of the amounts obtainable in well planned diets does not change the insulin requirement of well controlled diabetic subjects.

The table shows the thiamine content, in micrograms, of the standard diets for diabetic subjects used.

It may be that the benefit reported [1] from the administration of thiamine hydrochloride to diabetic patients has been assumed on the basis of the response of subjects whose disease was poorly controlled. Very possibly, the patient with poorly controlled diabetes may in addition have a true deficiency of vitamin B_1. If this is true, thiamine therapy should lead to a favorable response. Such a response would not establish an increased need for thiamine by the well stabilized diabetic patient, who already is receiving his requirement of the vitamin in his diet Recently it has been frequently pointed out that thiamine deficiency in man is more common than has been generally recognized and that unless careful consideration is given diets easily can be deficient in the components of the vitamin B complex. Patients with diabetes mellitus are in need of good diabetic regulation. This need is emphasized by the level of control frequently exhibited by patients used for investigation. It would be helpful to find some therapeutic short cut, but as yet none has been discovered.

SUMMARY

From the evidence offered it is concluded that the ingestion of vitamin B complex in amounts in excess of those obtainable in well planned diets did not lessen the insulin requirement of children with diabetes mellitus which had been previously well controlled.

SULFANILAMIDE IN THE TREATMENT OF ACUTE OTITIS MEDIA IN CHILDREN

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Since the advent of chemotherapy there have been many conflicting reports concerning its value, and even the advisability of its use, for the treatment of acute otitis media. The majority of these reports have been made by otologists, and few have been the expressions of pediatricians. Brennemann,[1] in his article entitled "Otitis Media as a Pediatrician Sees It," appropriately stated: "He [the pediatrician] and the general practitioner, alone, are in a strategic position to acquire extensive and practical knowledge of the developmental period of middle ear disease and a resulting ability to prognosticate with some assurance in an early questionable case." It is the general practitioner or the physician limiting his practice to the care of infants and children who not only is in a position to see patients with infections of the middle ear early but usually first institutes therapy. With this thought in mind, and from a purely pediatric point of view, the following discussion is presented.

In an effort to test the clinical efficacy of chemotherapy in the treatment of acute otitis media, it was decided to observe carefully a series of patients with this condition, of whom half were to be given sulfanilamide in addition to symptomatic treatment and half were to serve as controls, by receiving only symptomatic treatment.

This study includes all patients with acute infections of the middle ear admitted to the outpatient department of Children's Memorial Hospital between Jan. 15 and July 1, 1940. Patients with chronic and recurrent otitis media were eliminated from the series. Only those patients who were satisfactorily followed up until there was complete disappearance of symptoms and signs, including complications, are reported on here. There was no special selection of the patients in the two groups. The majority of the physicians on the clinical attending staff treated their patients symptomatically, while the resident staff mem-

From the Children's Memorial Hospital.

1. Brennemann, J.: Otitis Media as a Pediatrician Sees It, J. A. M. A. **97**: 449-451 (Aug. 15) 1931.

bers assigned to the clinic service administered sulfanilamide in addition to symptomatic care. Routine treatment consisted of: (1) application of heat to the affected ear, (2) use of ear drops (glycerite of phenol, 3 or 5 per cent), (3) use of dry cotton wicks to wipe away discharge when present, (4) myringotomy when definitely indicated (sustained fever, severe earache and bulging tympanic membrane) and (5) treatment of acute infections of the upper respiratory tract still present at the time of the acute aural involvement.

Patients receiving sulfanilamide were examined every one to three days. Dispensing of no more than the calculated three day dose insured return of the patient for continued observation and therapy. Only oral medication was prescribed. Dosage was figured on a basis of 15 to 20 grains per 20 pounds (0.97 to 1.23 Gm. per 9 Kg.) of body weight. This was maintained for the first three days and then either continued at the same level or gradually reduced, depending on the clinical response

TABLE 1.—*Distribution of Four Hundred and Twenty-Five Patients with Acute Otitis Media*

	(A) Otorrhea Absent	(B) Otorrhea Present	Total
Group 1: Patients treated with sulfanilamide	...	...	222
Subgroup 1A	108 (48.6%)		
Subgroup 1B		114 (51.4%)	
Group 2: Controls	...	...	203
Subgroup 2A	54 (26.6%)		
Subgroup 2B		149 (73.4%)	
Total			425

to the drug. In the group treated with sulfanilamide, the majority of the patients were given chemotherapy at the time of the first visit to the clinic. Administration of the drug was discontinued with the appearance of such unfavorable reactions as persistent vomiting or cutaneous eruptions or with the development of signs indicative of mastoid involvement. All patients with complications were admitted to the ear, nose and throat service of the hospital. Unfortunately, it was impossible for us to check the levels of sulfanilamide in the blood of the ambulatory patients.

An accurate description of both drum membranes and a report of the amount and the type of discharge, when present, were recorded at each visit. This record played an important part in facilitating an accurate estimation of the duration of illness and of otorrhea and the time elapsed between the onset of aural involvement and complete healing.

The patients in each series were divided into two groups: (A) those whose disease ran its course without perforation of the tympanic membrane and (B) those who had otorrhea, as a result either of myringotomy or of spontaneous rupture of the drum membrane. The investigation included 425 patients (table 1), of whom 222 were treated

with sulfanilamide and 203 were used as controls. In group 1, which consisted of the patients treated with chemotherapy, there were 108 patients who did not have an aural discharge (subgroup 1 A) and 114 who had definite otorrhea (subgroup 1 B). In group 2, the controls, there were 54 patients whose disease subsided without myringotomy or spontaneous rupture of the drum membrane (subgroup 2 A) and 149 whose ears drained (subgroup 2 B).

The ages of the patients varied from 2 weeks to 13 years. There were 227 boys and 198 girls in the series. Among the 425 patients included in the investigation 238 had involvement of both ears (133 in group 1 and 105 in group 2), so that 663 ears were treated.

The duration of illness in this series is interpreted as the total time elapsed between the onset of the first symptoms referable to the ear and the restoration of the drum membrane to normal and the cessation of otorrhea or complete healing of complications. The time elapsed between the onset of complaints referable to the ear and the initial administration of chemotherapy averaged 4.35 days. Among the controls, the duration of illness prior to the patient's first visit to the clinic was 4.15 days. The average total duration of aural involvement was 15.76 days for the group treated with sulfanilamide and 24.80 days for the controls, an average decrease of 9.04 days for the patients given chemotherapy. In computing these averages figures for the patients in both groups who had complications and were hospitalized for surgical procedures on the mastoid were included. For subgroup 1 A and subgroup 2 A, in which there were no patients with otorrhea, the duration of involvement was 10.63 and 12.83 days respectively, an average decrease in the total period of illness of 2.2 days for the patients treated with sulfanilamide. For subgroup 1 B (114 patients) and subgroup 2 B (149 patients), in which all of the patients had an aural discharge, the average duration of involvement was 20.64 and 29.17 days respectively, an average decrease in the period of illness of 8.53 days for the patients who received chemotherapy (table 2).

The average duration of otorrhea was 11.58 days for the patients given sulfanilamide and 20.43 days for the controls. This represents an average decrease in the period of aural discharge of 8.85 days for the patients given chemotherapy (table 2). Sixty-one, or 53.5 per cent, of the 114 patients in subgroup 1 B and 89, or 59.7 per cent, of the 149 patients in subgroup 2 B had an aural discharge at the time of the first examination.

The dosage of sulfanilamide in all cases was between ¾ and 1 grain per pound (0.045 and 0.06 Gm. per 0.5 Kg.) of body weight per twenty-four hour period. At first the twenty-four hour dose was given in six equally divided doses at four hour intervals. After the first three

days the drug was usually given four times daily, between 8 a. m. and midnight. The average total period of administration of sulfanilamide was 5.5 days. Medication was usually discontinued as soon as the normal drum landmarks became visible. Unfavorable reactions to the drug were not commonly observed during the course of this investigation. We encountered 14 reactions attributable to sulfanilamide which necessitated its withdrawal. There were 9 instances of persistent vomiting and 5 of generalized urticarial cutaneous eruption. Erythrocyte, leukocyte and differential blood counts were made for the children receiving chemotherapy for a period of six days or more, and no instance of severe anemia, leukopenia or granulocytopenia was discovered.

Specimens of the aural discharge were usually taken for culture at the time of the first visit, and the patients (in group 1) with a discharge

TABLE 2.—*Duration of Illness and Duration of Drainage in Four Hundred and Twenty-Five Cases of Acute Otitis Media*

	Number of Patients	Duration of Drainage, Days *	Duration of Illness, Days
Group 1: Patients treated with sulfanilamide	222	.....	15.77
Subgroup 1A	108	.....	10.63
Subgroup 1B	114	11.58	20.64
Group 2: Controls	203	.....	24.82
Subgroup 2A	54	.....	12.83
Subgroup 2B	149	20.43	29.17
Average decrease in duration in favor of groups receiving sulfanilamide therapy:			
Subgroup 1A over subgroup 2A		....	2.20
Subgroup 1B over subgroup 2B		8.85	8.53
Group 1 over group 2		....	9.05

* Otorrhea was present in subgroups 1B and 2B and absent in subgroups 1A and 2A.

were given chemotherapy routinely, before information as to the offending organism had been obtained. Cultures were made of material on the myringotomy knife in all cases in which this operation was performed. A total of 174 cultures were made. In table 3 the incidence of the various offending organisms is given. Beta hemolytic streptococcus and Staphylococcus aureus were found in combination in many of the cultures. The streptococcus in each case was considered the pathogen and the staphylococcus a contaminant.

Sustained fever, severe earache and bulging of the tympanic membrane served as indications for myringotomy. These requirements were met by and paracentesis performed on 33 patients in the group treated with sulfanilamide and 50 controls; this is an incidence of 14.8 and 24.6 per cent respectively, or a difference of approximately 10 per cent between the figures for the two groups. Of the 33 patients in subgroup 1 B on whom myringotomy was performed, 20 underwent the operation at the time of their first visit to the clinic, before chemotherapy had been instituted.

Probably the most significant result in this investigation was the difference in the incidence of complications in the two groups. Our statistics reveal 12 instances of surgically proved mastoiditis among the controls and only 4 among the patients given chemotherapy. Thus the incidence of complicating mastoiditis was 1.8 per cent in the group given sulfanilamide and 5.9 per cent among the controls, a difference

TABLE 3.—*Incidence of Offending Organisms in One Hundred and Seventy-Four Cultures in Cases of Acute Purulent Otitis Media*

			Number	Per Cent
Beta hemolytic streptococcus			89	51.25
Staphylococcus aureus			38	21.83
Pneumococcus			21	12.06
Type I	4	2.30		
Type II	1	0.57		
Type III	3	1.72		
Type V	4	2.30		
Type X	1	0.57		
Type XII	1	0.57		
Type XIV	2	1.11		
Type XVIII	2	1.11		
Type XIX	3	1.72		
Diphtheroids			10	5.74
Staphylococcus albus			3	1.72
Sarcinae			3	1.72
Hemolytic staphylococcus			2	1.11
Streptococcus viridans			1	0.57
Haemophilus influenzae			1	0.57
Colon bacillus group			1	0.57
Friedländer bacillus			1	0.57
Bacillus subtilis			1	0.57
No growth			3	1.72
			174	100.00

TABLE 4.—*Data for Patients in Groups 1 and 2 Who Underwent Myringotomy*

	Group 1 (Patients Treated with Sulfanilamide)	Group 2 (Controls)
Incidence of myringotomy	33 (14.8%)	50 (24.6%)
Incidence of mastoiditis (surgically proved)	4 (1.8%)	12 (5.9%)
Result of culture of material from mastoid:		
Beta hemolytic streptococcus	4	11
No growth	0	1
Fatalities	0	0

of 4.1 per cent in favor of the group given chemotherapy when the total number of patients in both series is considered. In other words, complicating mastoiditis was three times as prevalent among the controls as among the patients given specific treatment.

Cultures of material taken from the mastoid at the time of operation yielded a pure growth of beta hemolytic streptococcus for 15 patients and no growth for the 1 remaining patient (table 4).

There were no fatalities in either group of patients.

COMMENT

In reviewing the literature, one finds a definite difference of opinion as to the established value of sulfanilamide in the treatment of acute otitis media. Reports by Williams,[2] Smith,[3] Converse,[4] Scal,[5] Maybaum [6] and Babcock [7] have pointed out the shortcomings of the drug in the treatment of this condition. Williams,[2] in reporting a small series of cases, stated that there was an increased duration of aural discharge in the group treated by chemotherapy. Smith,[3] in discussing Williams' paper, stated: "We have not been able to abort otitis media with sulfanilamide or sulfapyridine. We are seeing in New York a great deal of harm done by the treatment of otitis media with these drugs." Converse,[4] in reporting on the recurrence of otitis due to beta hemolytic streptococcus, suggested that "sulfanilamide should be reserved for the treatment of spreading or life-endangering infections and that it should not be used as an adjunct to the usual measures for the treatment of infections of minor severity." Scal [5] has expressed the opinion that the drug is too treacherous to use as a therapeutic agent in the treatment of the early stages of aural conditions.

Maybaum [6] has called attention to the tendency of the drug to obscure the clinical course of the infection, and has expressed the belief that sulfanilamide should be used cautiously, if at all, in the treatment of acute otitis media. Babcock [7] has expressed the opinion that the effect of sulfanilamide in the treatment of acute infections of the ear is somewhat overrated.

Our statistics, however, tend to sustain the more favorable reports of Bowers,[8] Houser,[9] Fisher,[10] Horan and French,[11] Bilchick and

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2. Williams, H. J.: Diagnosis and Treatment of Diseases of the Ear in Children, J. A. M. A. **113**:990-993 (Sept. 9) 1939.

3. Smith, C. H., in discussion on Williams.[2]

4. Converse, J. M.: Recurrence of Otitic Infections Due to Beta Hemolytic Streptococcus Following Inadequate Sulfanilamide Therapy, J. A. M. A. **113**: 1383-1387 (Oct. 7) 1939.

5. Scal, J. C.: Evaluation of Sulfanilamide Therapy in Acute Otitis Media and Mastoiditis, New York State J. Med. **39**:1790-1794 (Sept. 15) 1939.

6. Maybaum, J. L.: Experience with Sulfanilamide Therapy for Otogenous Infections with Special Reference to Masking of Clinical Course, Arch. Otolaryng. **30**:557-575 (Oct.) 1939.

7. Babcock, J. W.: Role of Sulfanilamide in the Treatment of Acute Otitis Media, Arch. Otolaryng. **32**:246-249 (Aug.) 1940.

8. Bowers, W. C.: Observation on Seven Hundred and Ninety-Three Cases of Acute Purulent Otitis Media with Chemotherapy in Three Hundred and Ninety-Six Cases, J. A. M. A. **115**:178-181 (July 20) 1940.

9. Houser, K. M.: Sulfanilamide: Survey of Use in Acute Otitis Media, Laryngoscope **49**:825-832 (Sept.) 1939.

O'Kane,[12] Baker and Bradford [13] and Greenwood.[14] In 231 selected cases reported by Bowers,[8] the duration of otorrhea among the patients receiving chemotherapy was 9 days as compared with 17 days for the control group. Bilchick and O'Kane [12] reported that the average number of days of aural discharge after the onset of treatment was 7 for their patients treated with sulfanilamide and 12.6 for their controls. Our statistics referring to the total duration of otorrhea, from onset to complete disappearance of the discharge, showed 11.58 days for the specifically treated series and 20.43 for the controls, figures which compare favorably with those of the earlier observers.

In addition to being responsible for an obvious reduction in the period of aural discharge, one is led to believe that it may be safely assumed from our statistics that the decrease in the prevalence of otorrhea in the group treated with sulfanilamide was due to the early administration of the drug. In support of this statement it may be pointed out that the disease of only 54 (26.6 per cent) of a total of 203 patients treated symptomatically subsided without the appearance of an aural discharge, while 108 (48.6 per cent) of a total of 222 patients treated by chemotherapy recovered completely without myringotomy or spontaneous rupture of the drum membrane. Six and two-tenths per cent more of the controls had otorrhea at the time of their first visit to the clinic; however, subtraction of this figure still leaves a difference of 15.8 per cent in favor of the series treated with sulfanilamide, which may be attributed to the utilization of the drug.

In regard to complications, our statistics support the results of Horan and French,[11] Bowers,[8] Fisher,[10] Galloway,[15] Houser [9] and Greenwood,[14] all of whom reported a definite reduction in the incidence of surgically verified mastoiditis among their patients given chemotherapy. The decrease in incidence of 4.1 per cent reported here compares more favorably with the 5.3 per cent reduction reported by Bowers for his selected cases than with the 19 and the 61 per cent reduction reported by Horan and French [11] and Fisher [10] respectively.

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10. Fisher, G. E.: Sulfanilamide in Treatment of Otitis Media, J. A. M. A. **112**:2271 (June 3) 1939.

11. Horan, V. G., and French, S. G.: Prevention of Mastoiditis: A Survey of Six Hundred and Twenty-One Cases of Acute Otitis Media Treated with Sulfanilamide, Lancet **1**:680-682 (April 13) 1940.

12. Bilchick, E. B., and O'Kane, G. H.: Sulfanilamide in Otitis Media in Children, Laryngoscope **50**:197-201 (Feb.) 1940.

13. Baker, D. C., Jr., and Bradford, G. E.: Sulfanilamide Therapy for Acute Otitis Media and Acute Mastoiditis, Arch. Otolaryng. **29**:334-344 (Feb.) 1939.

14. Greenwood, G. J.: Practical Applications of the Sulphuramids to Otolaryngology, Illinois M. J. **78**:410-418 (Nov.) 1940.

15. Galloway, T. C.: Chemotherapy, Arch. Otolaryng. **30**:901-915 (Dec.) 1939.

Early in this investigation, the administration of sulfanilamide was always discontinued when the first signs of involvement of the mastoid appeared. However, at present we believe that whenever the presence of mastoiditis is suspected an otologist should see the patient immediately and that it should be left to the discretion of that specialist whether chemotherapy is stopped, temporarily discontinued or maintained at the same, or even a higher, dosage. Livingston [16] has reported 5 cases of mastoiditis in which all the indications for surgical intervention were present but the infection subsided completely with carefully administered chemotherapy. Greenwood [14] pointed out that "Early mastoiditis associated with an acute fulminating otitis media, such as is seen with invasion by the beta hemolytic streptococcus, is a pathological state amenable to adequate chemotherapy."

The majority of the advocates of this specific therapy for the treatment of acute otitis media have expressed the belief that to be of greatest value the drug should be given as early as possible. Probably the results of our observations would be even more favorable had there not been an average lapse of 4.35 days between the onset of the complaints referable to the ear and the initial administration of the drug. This figure certainly can be reduced considerably in private practice.

It has been the plan during recent months in the outpatient department of Children's Memorial Hospital to administer sulfanilamide to almost all patients with acute otitis media at the time of their first visit to the clinic. Sulfanilamide is the drug of choice because of the preponderance of hemolytic streptococcic infections of the ear. However, if after two or three days the reports on cultures show that the infection is due to some other organism or if there is no response to sulfanilamide, a more specifically indicated drug is promptly substituted. At present, a similar investigation is being made with sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole). A comparative statistical analysis of the clinical therapeutic value of this drug as compared with that of sulfanilamide, as given in this report, will go a long way in determining which form of chemotherapy is preferable in the treatment of the early stages of acute otitis media without aural discharge. For patients with otorrhea, the results of culture indicate the chemotherapeutic agent to be administered.

SUMMARY AND CONCLUSIONS

A statistical report of the results of treatment of 425 patients with acute otitis media is given. Two hundred and twenty-two children were

16. Livingston, G. S.: Sulfanilamide Therapy, Ann. Otol., Rhin. & Laryng. **46:** 1127 (Dec.) 1937.

treated with sulfanilamide and 203 served as controls. A total of 663 infections of the ear were observed and treated during the course of the investigation.

The total period of illness and the duration of otorrhea were decreased as a result of chemotherapy.

The incidence of otorrhea, myringotomy and complications requiring surgical care was materially reduced by administration of the drug.

As a result of this investigation, it is suggested that sulfanilamide therapy, under careful supervision, should be tried in all cases of acute otitis media and that the drug should be given early in the course of illness, in adequate dosage and over a sufficiently long period to insure against a recurrence of symptoms when it is discontinued.

When the presence of complications is suspected, the patient should immediately be examined by an otologist and the proper medical or surgical therapeutic measures promptly instituted.

BLOOD CELLS IN HEALTHY YOUNG INFANTS

IV. POSTNATAL READJUSTMENTS OF THE RED BLOOD CELLS IN INDIVIDUAL BABIES

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DENVER

Since these studies were started, in 1931, there have appeared a number of papers dealing more or less extensively with the changes in the red blood cells of healthy infants. Windle [1] recently published an interesting review on prenatal blood development and the changes in the blood picture at birth. The general picture after birth, together with the range of values at different age levels, has been presented most adequately in articles by Josephs,[2] Mugrage and Andresen,[3] Guest, Brown and Wing [4] and Faxén.[5] Several of these authors, notably Josephs and Faxén, have discussed postnatal adjustments and have included adequate bibliographies. Although the desirability of studying individual babies through the early weeks of life has been mentioned by a number of workers, there seems to have been a paucity of such material published. This fact serves as justification for adding to the overcrowded current literature further articles on the red cells in early infancy, of which this is the first.

From the Child Research Council and the University of Colorado School of Medicine.

Read in part at the meeting of the American Pediatric Society, Hot Springs, Va., May 22, 1941.

1. Windle, W. F.: Development of the Blood and Changes in the Blood Picture at Birth, J. Pediat. **18**:538 (April) 1941.

2. (*a*) Josephs, H. W.: Anemia of Infancy and Early Childhood, Medicine **15**:307 (Sept.) 1936; (*b*) The Mechanism of Anemia in Infancy: Physiological Anemia, Bull. Johns Hopkins Hosp. **55**:335 (Nov.) 1934.

3. Mugrage, E. R., and Andresen, M. I.: Values for Red Blood Cells of Average Infants and Children, Am. J. Dis. Child. **51**:775 (April) 1936.

4. Guest, G. M., and Brown, E. W.: Erythrocytes and Hemoglobin of the Blood in Infancy and in Childhood: I. Size and Hemoglobin Content of the Erythrocytes in Nutritional Anemia, Am. J. Dis. Child. **52**:616 (Sept.) 1936. Guest, G. M.; Brown, E. W., and Wing, M.: Erythrocytes and Hemoglobin of the Blood in Infancy and Childhood: II. Variability in Number, Size and Hemoglobin Content of the Erythrocytes During the First Five Years of Life, ibid. **56**: 529 (Sept.) 1938.

5. Faxén, N.: The Red Blood Picture in Healthy Infants, Acta pædiat. (supp. 1) **19**:142, 1937.

MATERIAL AND METHODS

The subjects were all healthy babies, born and cared for at the Florence Crittenton Home, in Denver (altitude, 5,000 feet [1,524 meters]). A detailed description of the nursery regimen was contained in the first paper [6] of this series and need not be repeated here, since there have been no significant changes. In the prenatal care given the mothers there has been some improvement in the dietary, the mineral intake and the general care, but their handling has been quite uniform during the period covered by the births of the 15 babies reported on in this paper. In the technic at delivery, also, several changes have been made during the ten year period. The only one of these which might affect the blood counts of the babies in any significant manner concerns the time at which the umbilical cord has been tied. Previous to March 1937 most of the babies' cords were allowed to stop pulsating before being tied. From March 1937 to September 1940 all cords were tied promptly after delivery. Since September 1940 all cords have been allowed to stop pulsating before being tied. That the time at which the cord is tied makes a difference in the baby's blood count is well known.[1] The results of these changes, however, will be the subject of a subsequent communication and need not be considered here except, possibly, as they may offer a partial explanation for the great range in cell counts at birth.

The 15 babies whose counts form the material for this report were all studied from March 1937 to May 1941. The cords of babies 1 to 5 were allowed completely to finish pulsating before being tied, while those of the other 10 infants were tied promptly after birth. Since the general mechanism of readjustment appears to be similar for both groups, they are considered together in this report. The duration and the regularity of the weekly counts for each of these 15 babies are shown in the table. Each weekly examination of the blood included the following determinations: red cell count, hemoglobin content, packed red cell volume, sedimentation time and reticulocyte count. White cell and differential counts on stained smears were also done, although the results are not reported here. The mean corpuscular volume, the mean corpuscular hemoglobin and the mean corpuscular hemoglobin concentration were calculated for each week's counts. A more complete report on the entire series of babies followed since 1931 will be published at a later date.

Although the various technical procedures are fairly well established, it may be well to include a few comments about certain points, since the reliability of the results are so largely dependent on the accuracy and the adequacy of the technics.

The red cell pipet was filled carefully from a free flowing heel prick. For the count the two sides of a double chamber were filled, some of the diluent being allowed to run out of the pipet before each side was filled. A completely new count was done on those rare occasions when there was a difference between the counts on the two sides of the chamber of more than 25 cells. Usually the counts on the two sides checked within 10 to 20 cells. Repeat counts on blood drawn from a fresh prick have been done occasionally when the first count seemed illogical or as a routine periodic check on the continued accuracy of my own

6. Washburn, A. H.: Blood Cells in Healthy Young Infants: II. The Leukocytic Picture During the First Three Months with Special Reference to Hourly and Daily Variations, Am. J. Dis. Child. **47**:993 (May) 1934.

technic. These have shown that the results check within a maximum difference of 200,000 cells in the final counts and, over half the time, within 125,000 cells.

The hemoglobin determinations have been performed with a Hellige solid standard hemoglobinometer. The instrument has been checked periodically against determinations of oxygen-carrying capacity with the Van Slyke apparatus, the hemoglobin determinations being corrected if necessary.

Packed red cell volume and sedimentation time have been determined with Smith hematocrit tubes,[7] but I used a somewhat different technic for filling them than that described by Smith.[7] The blood from a free flowing heel prick was collected in small vials containing heparin, as described by Andresen.[8] After thorough mixing it was transferred to the hematocrit tube with a capillary pipet. Sedimentation was observed every fifteen minutes for the first hour, then after one and a half, two and three hours. In about half the cases it was observed for as long as eight hours. Whether the hematocrit tubes were centrifuged at once or at varying intervals up to twenty-four hours made no difference in the readings of cell volume. The usual routine was to centrifuge and to read the cell volume eighteen to twenty-four hours after the tube was filled.

The checking of the reliability of the reticulocyte counts caused me the most anxiety and labor. The better part of sixty working days was spent in "ironing out the wrinkles" before satisfactory reliability was secured. The final technic, adopted in 1936, represents the result of: first, 50 duplicate counts made to compare different staining and spreading methods and, second, 104 counts done with the chosen method, in each of which at least 8,000 red cells were counted. In 33 of these preparations the number of reticulocytes found in counting 32,000 red cells was recorded. In making all of the reticulocyte counts reported in this paper the technic was constant. Dried, even and fairly heavy blue films were produced on clean slides by spreading out a few drops of a saturated alcoholic solution of brilliant cresyl blue. A small drop of blood from a free flowing heel prick was caught on a scrupulously clean cover slip, which was then inverted gently onto the cresyl blue film on the slide. This was sealed with petrolatum as soon as the blood had spread to the edges of the slip. Maximum staining of the reticulocytes was found to be present in twenty to thirty minutes and to remain constant for at least three hours at room temperature. At least 8,000 red cells were counted, in order to yield a reliable figure for reticulocyte percentage.

As in the earlier studies of this series, all of the counts and the other technical procedures were carried out by me.

RESULTS

Chart 1 shows curves for the various red cell values determined for baby 56 from birth through the thirteenth week of life. The downward trends in the curves for the red cell count, the hemoglobin content and the volume of packed cells are approximately, though not precisely, parallel during the first eight weeks. During this same period the curve

7. Smith, C. H.: A Method for Determining the Sedimentation Rate and Red Cell Volume in Infants and Children with the Use of Capillary Blood, Am. J. M. Sc. **192**:73 (July) 1936.

8. Andresen, M. I.: A Method for the Collection of Peripheral Blood Samples, J. Lab. & Clin. Med. **23**:751 (April) 1938.

for body weight progresses steadily upward. In contrast to these three curves, that for the reticulocyte count drops abruptly, during the first week, to a point which represents a figure too low to be consistent with maintenance of a normal number of red cells. As the red cell curve descends the reticulocyte curve begins to rise again. As the red cell

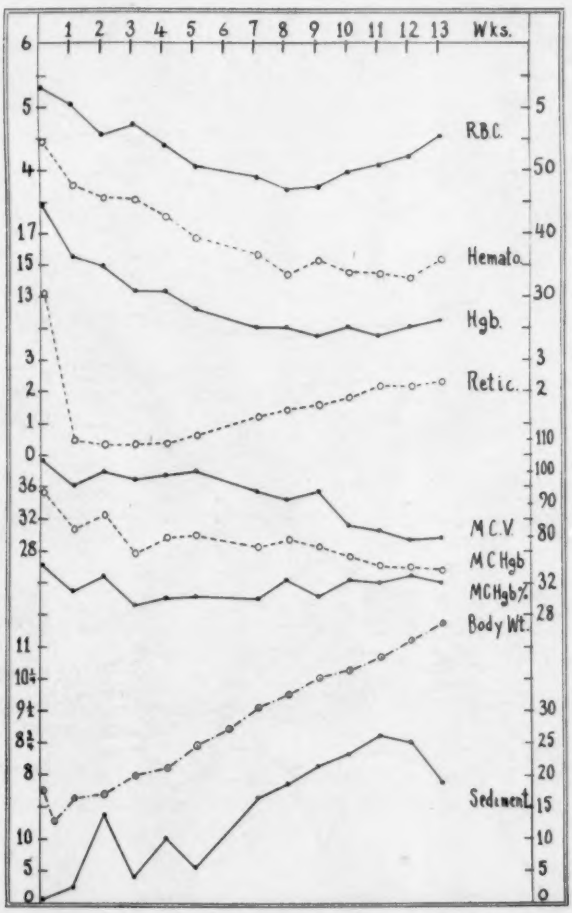

Chart 1.—Curves of red cell values for baby 56, illustrating the various postnatal changes studied. (Compare with chart 2.)

count starts increasing after eight weeks, the body weight continues to increase and the reticulocyte count remains well above the probable maintenance level of about 1.0 per cent. Meanwhile, in the latter period, the curves for packed red cell volume and hemoglobin content do not parallel the curve for the red cell count but remain more nearly horizontal, while the mean corpuscular size decreases.

In chart 2 similar curves are presented for the same red cell values of baby 43, who was followed from birth to 17 weeks of age. A comparison of these curves with the corresponding ones in chart 1 brings out some interesting differences, even though, in general, the trends are similar. The most striking changes are seen in the rate of decrease of

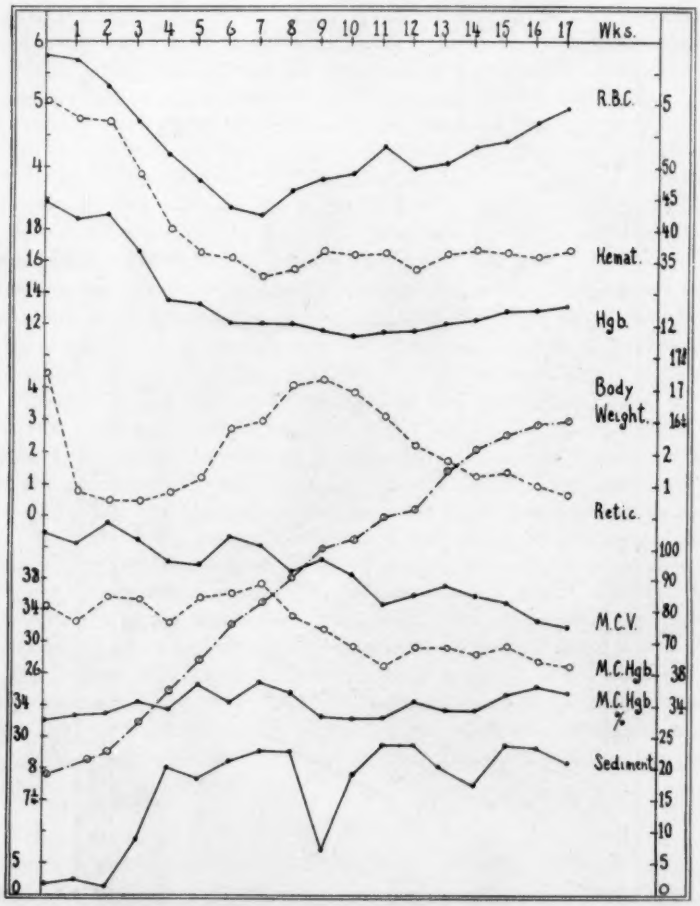

Chart 2.—Curves of red cell values for baby 43, to be compared with the curves in chart 1. (See text.)

the red cells, the rate of increase of the body weight and the size of the reticulocyte response. The low point of the red cell curve occurs at 6 weeks of age for this baby, in contrast to a low point at the age of 8 to 9 weeks for the former infant. The percentage decrease is 44 per cent for baby 43 and only 29 for baby 56. The body weight of the second baby increases by 50 per cent in the first six weeks, whereas that of the first

baby increased only 30 per cent in eight weeks. And, finally, the peak of the reticulocytes for baby 43 is twice as high as that for baby 56, and it occurs at an earlier date.

The observation of such contrasting results for many different babies suggested a somewhat simplified presentation of the picture of postnatal readjustments of the red blood cells. This concept is based on the data, contained in the table, on 15 representative babies whose follow-up records were reasonably complete and uniform and who all remained in good health.

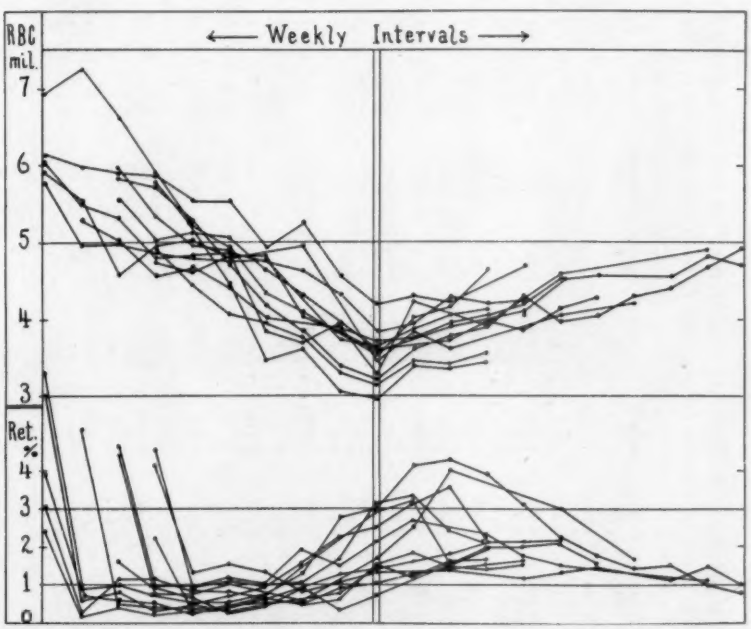

Chart 3.—Curves of red cell and reticulocyte counts for 12 babies superimposed at the point of lowest red cell count, which was reached at the ages of from 6 to 9 weeks by the different babies.

In chart 3 I have superimposed the curves of the red cell counts for 12 of these babies, using the lowest value on the curve as the point of superimposition rather than the chronologic age. Although this is a somewhat arbitrary maneuver, it seems quite logical, since this value represents a sort of critical turning point, at which the production of new red cells has become active enough to start the red cell count on its upward path. It is, approximately, the midpoint in the period of readjustment, which is usually fairly well finished in another six to nine weeks, when a fair degree of equilibrium is established in the majority of babies. The reticulocyte curve for each baby is drawn in to match

Red Cell Counts (in Millions per Cubic Millimeter), Reticulocyte Counts (in Percentage) and Body Weights (in Pounds and Ounces) of Fifteen Healthy Infants During the First Three Months of Life

Age, Weeks	Infant 43	Infant 48	Infant 49	Infant 50	Infant 51	Infant 54	Infant 55	Infant 56	Infant 57	Infant 61	Infant 62	Infant 1	Infant 3	Infant 4	Infant 5
0	5.776	...	...	5.576	5.760	...	...	5.280	6.040	4.700	5.800	6.120	6.992	7.108	...
	4.4	...	...	4.6	6.0	...	...	5.1	3.0	4.1	3.9	6.5	2.5	3.4	...
	7-14	7-2	7-2	7-14	8-3	5-2	6-2	7-10	6-0	7-7	6-6	8-3	8-1	8-2	7-2
1	5.712	5.992	4.464	5.032	4.924	5.724	4.700	5.036	5.520	4.680	5.560	5.968	7.288	5.780	5.920
	0.8	1.6	1.4	0.9	0.5	2.2	4.5	0.5	0.3	1.3	0.9	0.7	0.2	0.1	0.9
	8-3	7-6	7-5	8-3	...	5-0	6-0	7-7	6-5	7-3	6-7	8-0	7-8	8-3	7-0
2	5.264	5.336	5.060	5.100	5.000	5.248	4.460	4.580	5.300	4.788	4.592	5.860	6.620	6.504	4.972
	0.5	1.0	0.6	0.6	0.8	0.4	0.8	0.4	1.1	1.5	1.0	0.5	0.4	0.2	0.3
	8-6	7-10	7-9	8-2	8-10	5-2	6-1	7-8	6-12	7-8	6-14	8-8	8-0	8-13	7-8
3	4.688	4.928	4.320	5.060	4.820	4.460	4.080	4.720	4.780	4.536	4.948	5.840	5.848	5.820	4.528
	0.5	0.8	0.5	0.3	0.3	0.7	1.1	0.4	1.1	1.3	0.8	0.4	0.2	0.2	0.9
	9-1	7-13	8-8	8-4	9-0	5-13	6-0	7-15	7-8	7-11	7-6	8-13	8-4	9-3	8-0
4	4.180	4.180	4.120	4.608	4.808	3.484	3.964	4.400	4.840	4.044	5.032	5.564	5.316	5.044	4.396
	0.8	0.8	0.5	0.5	0.4	0.9	1.0	0.4	0.8	0.8	0.8	0.2	0.3	0.1	0.6
	9-13	8-4	8-12	8-5	9-5	6-6	6-7	8-2	8-2	8-2	7-8	9-8	8-12	9-13	8-7
5	3.812	3.796	3.672	4.292	4.540	3.600	3.740	4.020	4.852	3.888	4.752	5.568	4.916	5.008	3.980
	1.2	1.0	0.7	0.9	0.3	1.5	1.0	0.7	0.8	1.1	1.0	0.4	0.3	0.2	1.3
	10-9	8-8	9-6	8-14	9-9	6-12	6-13	8-11	8-2	8-6	7-13	9-13	9-4	10-3	8-13
6	3.372	3.648	3.744	3.920	4.500	3.076	3.300	...	...	3.668	...	4.812	4.296	4.952	3.760
	2.8	1.9	1.3	0.3	0.5	2.2	1.6	...	...	1.4	...	0.6	0.7	0.6	1.5
	11-7	9-0	9-15	9-4	9-11	7-7	7-8	9-1	8-4	8-10	7-7	10-0	9-14	10-10	9-2
7	3.220	3.980	3.848	3.620	...	2.924	3.220	3.888	4.692	...	4.952	5.292	4.060	4.684	3.700
	3.0	1.4	0.9	0.7	...	2.5	3.0	1.2	0.5	...	0.5	0.5	1.4	0.9	2.6
	11-14	9-10	10-8	9-2	...	7-12	7-13	9-9	8-5	9-1	7-11	10-2	10-4	11-0	9-9
8	3.640	3.250	3.110	...	3.740	3.400	3.460	3.700	4.360	3.966	...	4.560	...	4.288	3.528
	4.1	2.1	1.3	...	0.8	3.2	2.1	2.1	0.6	1.4	...	0.9	...	0.8	2.4
	12-11	9-14	11-1	9-0	10-6	8-1	8-4	9-15	8-11	9-6	8-5	10-7	10-10	11-8	9-15
9	3.788	4.280	3.844	3.712	3.692	3.360	3.412	3.732	3.840	...	3.480	4.220	3.584	4.468	3.832
	4.2	2.6	1.4	1.4	1.4	3.6	2.4	1.6	1.4	...	1.7	1.0	3.0	1.8	2.5
	13-3	10-2	11-7	9-0	10-14	8-6	8-12	10-4	9-4	9-8	8-14	10-10	11-4	11-14	10-4

10	.....	3.874	...	...	4.040	3.800	3.376	3.552	3.988	3.928	4.184	3.856	4.336	4.020	4.524	3.820
		3.9	...	...	2.2	1.2	2.1	1.6	1.8	1.8	1.1	2.5	1.2	3.2	1.5	3.3
		13-6	...	...	9-8	10-14	8-12	9-4	10-6	9-12	9-14	9-0	10-14	11-7	12-9	10-8
11	.....	4.320	4.000	4.280	3.824	4.096	...	...	4.048	4.364	4.508	3.608	4.280	4.224	4.784	3.956
		3.1	2.1	1.6	2.0	1.6	...	...	2.1	1.5	1.2	4.0	1.4	1.5	2.1	4.1
		14-0	10-8	11-12	9-13	11-6	...	...	10-13	9-14	9-12	9-7	11-6	11-7	12-13	11-0
12	.....	3.940	4.148	3.904	4.120	4.140	...	...	4.216	4.200	4.556	...	...	4.632	5.084	4.144
		2.2	1.7	1.8	2.1	1.6	...	...	2.1	1.4	1.3	...	...	2.0	1.6	2.2
		14-3	11-0	12-3	10-4	12-1	...	...	11-3	10-4	10-2	10-0	11-10	11-9	13-5	11-2
13	....	4.056	4.592	...	4.240	...	...	...	4.520	4.288	...	...	4.716	...	5.428	4.448
		1.8	1.4	...	1.4	...	...	...	2.2	1.5	...	...	1.5	...	1.4	1.9
		15-5	11-6	...	10-4	...	...	...	11-9	10-12	10-6	...	12-1	...	13-15	11-9
14	....	4.300	...	...	...	...	...	...	...	...	4.520	4.040	...	...	5.044	...
		1.4	...	...	...	...	...	...	...	...	1.1	3.0	...	...	1.3	...
		15-10	...	...	...	...	...	...	...	...	10-10	10-12	...	...	14-5	...
15	.....	4.396	...	...	...	...	...	...	...	...	4.880	...	...	...	4.860	...
		1.5	...	...	...	...	...	...	...	...	1.4	...	...	...	1.1	...
		15-15	...	...	...	...	...	...	...	...	11-4	11-3	...	...	14-12	...
16	.....	4.676	...	...	...	...	...	...	...	...	4.624	4.440	...	...	5.580	...
		1.0	...	...	...	...	...	...	...	...	1.0	1.7	...	...	0.9	...
		16-2	...	...	...	...	...	...	...	...	11-8	12-1	...	...	14-15	...
17	....	4.920	4.812	...	...	...	...	...	...	...	...	...	...	...	5.904	...
		0.7	...	...	...	...	...	...	...	...	...	...	...	...	1.0	...
		16-4	13-2	...	...	...	...	...	...	...	...	...	...	...	15-0	...

its corresponding red cell curve. Thus the variation of three weeks in the start of these curves actually represents the difference in the rate of descent of the red cell counts of different babies.

If one observes all of the curves to the left of the double center line, it will be noted that the red cell counts are all showing a nearly continuous decrease while the majority of the reticulocyte counts are less than 1 per cent, excluding the initially high start of each curve. By contrast, when one looks only at the curves to the right of the vertical lines, prac-

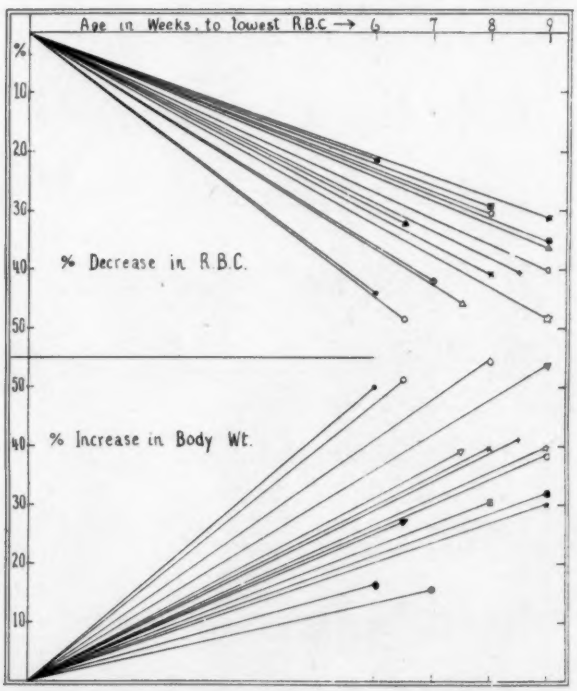

Chart 4.—Comparison of the percentage decreases in red cell counts with the percentage increases in body weight for 15 babies. Symbols permit one to match the appropriate pair of curves for each baby.

tically all of the reticulocyte values are seen to lie above 1.0 per cent, while a good many scatter out between 2.0 and 4.2 per cent. During this period most of the red cell curves are showing a fairly consistent rise from week to week. Although this method of charting results gives a more uniform picture than when chronologic age is used there are apparent inconsistencies even here. For instance, some of the reticulocyte curves are above 1.0 per cent well before the low point of the red cell count is reached, while others rise just at this point. Moreover, there is

a striking difference in the degree of reticulocyte response of different babies, as is noted by comparing charts 1 and 2. A study of these differences led to a comparison of the decrease in red cells and the increase in weight during the first six to nine weeks.

Such a comparison is made for all 15 babies in chart 4. Here each line in the upper one half of the chart represents the percentage decrease in the red cell count for 1 baby, from the initial count to the lowest. The age at which the lowest count was recorded is included, so as to yield a picture of the rate of decrease as well as its extent. In the lower half of the chart each corresponding line represents the percentage increase in

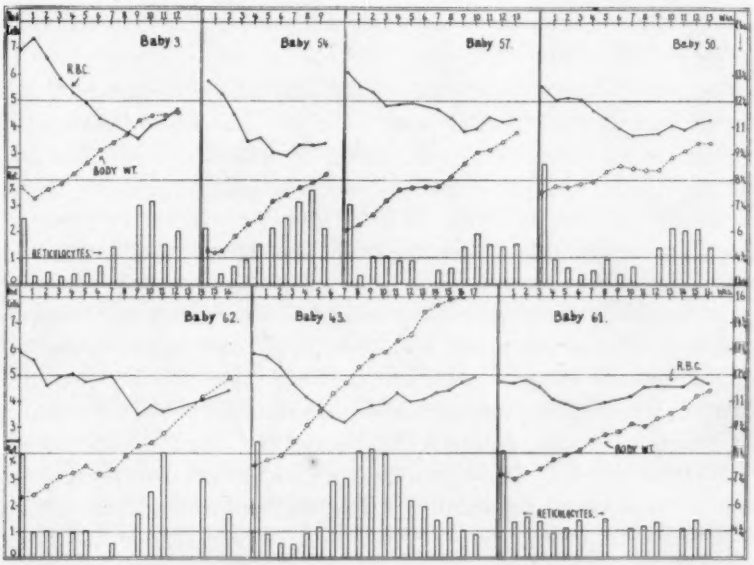

Chart 5.—Illustration of the interrelation of changes in (1) number of red cells per cubic millimeter, (2) total body mass and (3) reticulocyte level for 7 babies who are representative of the 15 studied.

body weight from the weight at birth to that recorded at the time of the lowest red cell count. Curves belonging to the same baby are indicated by identical symbols at their divergent ends. Eleven of these 15 pairs of curves are within 6 per cent of each other, while only 3 showed marked differences. After studying charts 3 and 4 it seemed probable that the charting together of the changes in red cell count, reticulocyte count and body weight for each individual baby would give the clearest picture of the necessary readjustments which are taking place. This procedure turned out to be helpful.

Chart 5 illustrates such a combination of data for 7 of the 15 babies, chosen as representing fairly the whole group. Babies 3 and 54 demon-

strate most simply the relation between the increasing body weight, the decreasing number of red cells and the acceleration in the rate of production of new red cells as the total number of erythrocytes drops rapidly below 4,000,000 per cubic millimeter of blood. Infants 57 and 50 are 2 of the 3 babies whose paired curves on chart 4 show the greatest discrepancy in percentages. The interesting inverse relation between the curves for red cell count and body weight stand out clearly on chart 5, in spite of the differences noted in chart 4. In the first of these the weight gain was proportionately greater than the red cell decrease. The mild reticulocyte increase at 2 to 4 weeks of age suggests a partial explanation for this. For baby 50 the adequate reticulocyte response occurred rather late, and the red cells decreased at a rate more rapid than that of the increase in body mass.

The curves depicting the changes for baby 62 are of particular interest. In the first nine to ten weeks there are similarities between these irregularities and those shown by babies 50 and 57. In the last six to eight weeks the red cell count increases steadily in spite of a rapid and steady increase in body weight. The reticulocyte response was marked during this time, reflecting a rapid enough increase in the manufacture of red cells to produce a steadily increasing number per cubic millimeter in spite of the rapid gain in weight. Baby 43 showed the steepest curves for both red cell count and body weight and, quite logically, the most marked and sustained increase in reticulocytes. By way of contrast, the curves for baby 61 illustrate the slowest changes in red cell count and body weight. It should be noted that the red cell count at birth was only 4,700,000 for this baby. The fact that the reticulocyte percentage for this infant never dropped significantly below the maintenance level suggests the presence of a protective mechanism guarding against too great a drop in the number of red cells. Certainly, 2 different babies may show striking differences in the whole pattern of readjustment, as is demonstrated by infants 43 and 61.

COMMENT

The data presented in charts 3, 4 and 5 lead one almost inevitably to a rather simple explanation of the mechanism involved in the striking changes in the red cells after birth. As the total body mass increases rapidly—increasing, occasionally, as much as 50 per cent in six weeks or 100 per cent in fourteen weeks—there is, presumably, a somewhat similar increase in total blood volume. In order to maintain a constant number of red cells per cubic millimeter of blood, the infant would have to manufacture new red cells at a rate considerably faster than that ordinarily needed to maintain the balance at a time when there was no sharp increase in body size. Most infants show an abrupt postnatal drop in their reticulocyte count, to 0.2 to 0.8 per cent. If one may

assume that normal maintenance of the red cell level is reflected by the presence of about 0.8 to 1.2 per cent reticulocytes, then it is obvious that most infants are not manufacturing new cells fast enough to maintain a constant level of red cells even when there is no great increase in blood volume. Consequently, as long as the body weight continues to rise and the reticulocyte percentage to remain low, the red cell count, the volume of packed cells and the amount of hemoglobin must necessarily decrease. And the more rapid the increase in total body mass, the more rapid would be the decrease in the number of cells per cubic millimeter of blood. Eventually, one would expect the decreasing concentration of red cells and hemoglobin to cause a stimulation of the hematopoietic tissue, most simply conceived of as resulting from a lack of oxygen. Hence, one is not surprised to observe the reticulocyte response or to note that it is usually most pronounced in those babies who show the most rapid decreases in red cell count and hemoglobin concentration. Then, when the number of red cells per cubic millimeter of blood has reached an optimum level for the individual baby's own body economy, the reticulocytes return to an approximate maintenance level of about 1.0 per cent, the exact level varying with the individual baby and even varying from time to time in the same infant.

This is, I realize, too simple an explanation to account for all the phenomena which may be observed, but as a general working hypothesis I believe it is essentially sound. Moreover, it appears to fit the majority of observed facts more logically than any other hypothesis. It is, nevertheless, obvious that I lack a number of important bits of evidence for its support. In the first place, I have made no determinations of blood volume. Such determinations on infants as are available in the literature [9] lead one to believe that plasma volume shows a definite increase in terms of the number of cubic centimeters per kilogram of body weight during the first six months. The evidence presented also suggests that the total blood volume per unit of body weight at least shows no decrease. In the most recent, and probably the most reliable, report on the blood volume of infants and children, by Brines, Gibson and Kunkel,[10] it is demonstrated that there is an almost constant relation between total blood

9. Bakwin, H., and Rivkin, H.: The Estimation of the Volume of the Blood in Normal Infants and Infants with Severe Malnutrition, Am. J. Dis. Child. **27**: 340 (April) 1924. Darrow, D. C.; Soule, H. C., and Buckman, T. E.: Blood Volume in Normal Infants and Children, J. Clin. Investigation **5**:243 (Feb.) 1928. Robinow, M., and Hamilton, W. F.: Blood Volume and Extracellular Fluid Volume of Infants and Children: Studies with an Improved Dye Micro-Method for Determination of Blood Volume, Am. J. Dis. Child. **60**:827 (Oct.) 1940.

10. Brines, J. K.: Gibson, J. G., II, and Kunkel, P.: The Blood Volume in Normal Infants and Children, J. Pediat. **18**:447 (April) 1941.

volume and body weight up to a weight of about 15 Kg. (33 pounds) with a subsequent increase in the number of cubic centimeters of blood per kilogram. These authors have shown that during the same period there is a steady increase in total blood volume per unit of height. Although this is suggestive evidence in support of my hypothesis, complete proof would require determinations of blood volume repeated at regular intervals on the same babies during this age period.

In the second place, I have made no mention of the possibility of an increased rate of destruction of red cells. I have not attempted to estimate the rate of red cell destruction by such measures as the rate of excretion of urobilin or the amount of bilirubin in the serum. Josephs [2a] has pointed out that in his extensive studies on the excretion of urobilin "a close correlation between fall in haemoglobin and urobilin excretion was not obtained." Waugh, Merchant and Maughan [11] have shown "that no relationship exists either between the individual total fall in hemoglobin and volume of packed red cells and the amount of bilirubinemia during the 9 days studied or between the changes in hemoglobin and volume of packed red cells and the total bilirubin concentration on any particular day." In spite of a number of similar statements to be found in the recent literature, almost every author, including those quoted, has assumed that an increased destruction of red cells is "obviously" taking place or is "largely responsible" for such features as the decrease in the red cell count and hemoglobin concentration, the bilirubinemia and the somewhat erratic increases in the excretion of urobilin. Faxén [5] is one of the few who have expressed skepticism; he has expressed the belief that more emphasis should be put on growth and the changing function of the bone marrow during the period of readjustment. Waugh, Merchant and Maughan [11] stressed "variations in the ability of the liver cells to excrete the excessive bilirubin transported to them" as an explanation of the bilirubinemia. If the blood volume does increase sufficiently and the rate of new cell formation does decrease enough to account, jointly, for the drop in the concentrations of red cells and hemoglobin per unit of blood during the first six to ten weeks of life, then it seems that one must seek some other explanation for the increases in bilirubinemia or in the excretion of urobilin than that of an abnormal rate of cell destruction. In any case, increased cell destruction is probably no more than a transient phenomenon, of brief duration.

There is, to be sure, evidence of considerable variation in the stability of the balance between cell production and cell destruction in different

11. Waugh, T. R.; Merchant, F. T., and Maughan, G. B.: Blood Studies on the Newborn: II. Direct and Total Blood Bilirubin; Determinations Over a Nine Day Period with Special Reference to Icterus Neonatorum, Am. J. M. Sc. **199**:9 (Jan.) 1940.

babies or in the same baby from time to time during the early weeks of life. Thus, the number of reticulocytes required to start an increase in the number of red cells per cubic millimeter varies from just over 1.0 per cent to approximately 3.0 per cent (chart 3). If this figure is expressed in terms of the actual numbers of cells per cubic millimeter needed it is not so striking but still ranges from 45,000 to 100,000, with a centering of the figures at about 55,000. Moreover, during the early weeks an occasional baby may show a very sharp drop in the red cell count without any correspondingly sharp rise in body weight. I have been inclined to blame such abrupt changes on the instability of the infant's mechanism for the adjustment of water balance and of plasma volume rather than on any sudden changes in the rate of cell destruction. It would be difficult, however, to rule out such changes as a possible contributing factor, especially in those occasional cases in which the blood picture is on the borderline between "normal variation" and a real anemia of the newborn.

In offering a simple hypothesis to explain the postnatal readjustment in the red cell values, I have not offered any reason for the very sharp postnatal drop in the percentage of reticulocytes. It seems doubtful, in the light of work which has recently been reported,[1] whether the high percentage present at birth is really dependent on a lowered availability of oxygen in utero. It may be, rather, a reflection of the great demands being made for new red cells by the rapidly growing organism. This does not rule out the possibility that the actual stimulus for the demand might still be lack of oxygen, but it does place the emphasis on a different fundamental cause. The stimulus may be lost with the immediate retardation of weight increase which usually follows birth. This would still fail to explain why such a prolonged drop in the red cell count and the hemoglobin concentration occurs before there is again any adequate stimulus to increased cell production. It seems possible that there is some unknown factor concerned with hematopoiesis which is available to the baby before birth, not available immediately after birth but present again at about 5 to 8 weeks of age.

SUMMARY AND CONCLUSIONS

A description is given of the postnatal readjustments in the red cell values of 15 healthy infants during the first ten to eighteen weeks of life.

The simple explanation advanced for the observed changes is based on the comparison of the weekly values for the red cell count, the reticulocyte count and the body weight for each individual baby. The comparison led to the conclusion that the decrease in the red cell count, the hemoglobin content and the volume of packed cells in the first six to nine weeks of life is dependent largely on two factors.

The first factor is the rapid increase in total body mass. This appears to involve a similar rate of increase in total blood volume, so that the ensuing dilution results in fewer red cells per cubic millimeter of blood.

The second factor is the abrupt decrease in reticulocytes, indicating a sudden decrease in the rate of production of red cells. In most babies the rate of production between the ages of 1 week and 5 or 6 weeks appears to be too low for maintenance of the red cell level in the blood, especially in the presence of an increasing plasma volume.

The decrease in the number of red cells and in the amount of hemoglobin per cubic millimeter of blood results in a rise in the reticulocyte percentage at about the fifth to eighth week. The sharpness and the persistence of the rise in different babies vary, roughly, with the rapidity of weight gain and the speed of decrease in the red cell count.

In most babies the red cell count starts to increase between the sixth and the tenth week of life and continues to rise until it reaches a level of between 4,500,000 and 5,500,000 at about 16 weeks of age. Meanwhile, the number of reticulocytes decreases to approximately 1.0 per cent.

It seems probable that the period of postnatal adjustment of the red blood cells, for most healthy babies, extends over the first fifteen to twenty weeks of life.

DISCUSSION

DR. A. ASHLEY WEECH, New York: I should like to ask a question which arises from an interest in the phenomenon of icterus neonatorum. Several years ago Book, in Winnipeg, Manitoba, Canada, reported that the frequency of physiologic jaundice depends on the procedure adopted with regard to the tying of the umbilical cord. When the cord is clamped immediately after birth, the incidence of jaundice is relatively low. When tying of the cord is delayed until all pulsations in it have ceased, the frequency of jaundice is relatively high. The difference was related to an excessive volume of blood squeezed into the infant's circulation when time is allowed for contraction of the uterus after expulsion of the fetus. I should like to ask Dr. Washburn whether he has any comments to make about the possible influence of this phenomenon on the erythrocyte counts and the hemoglobin levels of newborn infants.

DR. GEORGE M. GUEST, Cincinnati: Usually too little attention is paid to the fact that the concentrations of various constituents of the blood may be in process of rapid change from the values determined at a given moment. Just as a concentration of 100 mg. of sugar per hundred cubic centimeters of blood has a different significance when the blood sugar is rapidly decreasing and when it is rapidly increasing, so a given red cell count may have a different significance when the number of erythrocytes is stationary than when it is decreasing and when it is increasing. Dr. Washburn's studies help to define the order of the hematologic changes which may be regarded as within normal limits during the neonatal period; these studies lead, however, to further questions concerning the physiologic mechanisms concerned in such changes. I should like him to indicate what hematopoietic factors may be responsible for the remarkable decreases and increases in red cell and reticulocyte counts which are observed in this age period. Granting that the digestive tract is concerned with the manufacture of the erythrocyte maturation factor as well as with the absorption and the utilization of iron, the

sharp hematologic changes observed at the age of about 3 months may denote some important adjustments in other phases of the infant's nutrition at that time.

DR. LOUIS K. DIAMOND, Boston: In a period when many studies concerned with the changes in blood cells and blood levels in infants have been carried out Dr. Washburn's work is outstanding in several ways. In the first place, there are few such studies of individual infants. Most measurements have been made on groups of infants and then averages taken as an estimate of what the individual normal should be. Another important factor which makes his paper unique is that the measurements have been carried on over a long period by a single well qualified person, and therefore the variations due to individual errors in technic of different technicians have been minimized. That this factor is important has recently been stressed by Strauss, in Boston, who has found what a tremendous error may exist in the enumeration of erythrocytes by the usual method when such measurements are carried out by different (though qualified) technicians. His study was on patients with pernicious anemia, and he found that differences in determinations of the erythrocyte level as ordinarily carried out might be as great as 1,500,000 in a count of 5,000,000.

One refinement in technic which may help to minimize such errors is the use of the photoelectric cell colorimeter, which has recently been employed in the measurement of cell opacity, which, in turn, is directly related to the number of cells and the cell size. My associates and I have followed up these measurements, especially those for prematurely born infants, and have found that Dr. Washburn's concept is of great importance. The prematurely born infant grows so much more rapidly than the full term infant and has such a rapidly expanding blood volume that a profound anemia develops invariably between the sixth and the twelfth week. By correlating the rate of increase in body weight and probably, therefore, the increase of blood volume with the reticulocyte response, an index of hematopoietic activity, as well as with the red cell counts or cell opacity measurements, we have obtained a clearer picture of the reasons for the development of the anemia of prematurity.

DR. ARTHUR F. ABT, Chicago: Some years ago I studied the anemia of premature infants, and, of course, in those days the photoelectric colorimeter did not exist. I do not think one needs a photoelectric colorimeter for every test. Personally, I believe one can count red cells rather accurately in a counting chamber. The premature infants I studied were divided according to the age of gestation and, naturally, according to weight; the older, heavier babies were called immature infants, for want of a better term, and those who were younger and lighter were simply referred to as infants.

Obviously, at birth the premature babies weighed less than the immature infants, and their red cell counts and hemoglobin concentrations dropped more rapidly and stayed down longer than did those of the immature infants; but when they started to gain in weight the values for hemoglobin and red cells also rose rapidly, as Dr. Washburn has shown, so that at about the fourth or fifth month the group of premature infants had caught up with the immature group.

I also studied the reticulocytes of these premature and immature infants and found a slight rise, similar to that found by Dr. Washburn for the full term babies. At that time, I was influenced by what I had read about pernicious anemia; it was believed then that if patients with that disease who were being fed liver had reticulocyte counts under 15 or 20 per cent their response to therapy was ineffectual. Consequently, at that time I placed little emphasis on a moderate reticulocyte count for the infants studied.

There seems to be a parallel between the features of premature and full term infants, especially with regard to blood volume. The premature infant differs, in part at least, from the full term infant because he undergoes relatively more rapid growth, and he should therefore have a more rapidly increasing blood volume, with a greater demand for the formation of red cells. The increased decline in

the values for red blood cells and hemoglobin for the premature and the immature infant, as compared with those for the full term infant, may therefore be explained by physiologic factors peculiar to prematurity.

Dr. Donovan J. McCune, New York: I should like to ask Dr. Washburn whether he has any speculations to explain why the generation of red cells does not keep pace with the enlargement of blood volume and whether he regards the lack of correlated growth to be a physiologic or a pathologic phenomenon. I should like to ask, in addition, whether he has data on the influence of the administration of iron or other food factors on the correlation of the two rates of development.

Dr. Alfred H. Washburn, Denver: In answer to Dr. Weech's question about clamping of the cords, I was a little slow to realize the significance of the time at which the cord was clamped; so my early figures (those obtained previous to about two years ago) were not at all concerned with the exact time of clamping the cord. Fortunately, I know at exactly what point the obstetrician came on the service who was almost vehement on the subject of clamping all cords just as soon as possible after the babies were born. That practice was stopped and for almost a year now all the cords have been allowed to stop pulsating before they are clamped; so I shall eventually have comparative figures.

These data are interesting (slide), because they are for the only baby in that earlier group whose cord was allowed to stop pulsating before it was tied. So far I have data on about 10 infants whose cords have been allowed to stop pulsating, and apparently the mechanism of readjustment of the erythrocytes is similar for all the infants studied, regardless of the time of clamping of the cord. The initial levels may be different, but the general mechanism is the same.

I think that the same general idea is back of the questions by Dr. Guest and Dr. McCune; so I shall answer them together. Why is the reticulocyte count high at birth? Why does it drop sharply after birth? Why does it not begin to rise more rapidly after the red cell count decreases, and what makes it start to rise again? I wish I knew the answers to all those questions. By way of hypothesis, it seems logical to me to assume that one important factor, perhaps the most important but not necessarily the entire explanation, for the high reticulocyte count at birth is the extremely rapid rate of growth of the fetus in the uterus with great demands being made for new red blood cells. The sharp drop after birth is perhaps partly associated with a very temporary slowing down of the growth process, but I think that is by no means the entire explanation. The lag in reticulocyte response after the red cell count has started to decrease has been puzzling me for a long time. Some investigators, of course, base the whole explanation for variation in the speed of manufacture of red cells on the amount of oxygen available to the blood-forming tissues. A fairly good case can be made out for this theory, but my own feeling is that there is some other factor, as yet not discovered, which might be called "X," which is available to the baby up to the moment of birth, is not available to him immediately after birth and does not come into the picture again until he is approximately 5 to 9 weeks of age. Whether, as I think Dr. Guest wanted to suggest, it is associated with activity of the stomach I do not know. I have no data either to support or to refute that particular point.

I have done no work on premature babies for about twelve or fifteen years, and I am certainly not competent to talk about the changes which occur in premature infants or to compare them with the changes in full term babies. As far as I could gather from the comments on the question of blood counts for premature infants, the discussers seem to think that the changes in premature infants are the same as those which occur in full term infants but they take an exaggerated form. I might say that in looking through the literature, not exhaustively but fairly thoroughly, the only comments I found which suggested this same explanation for the changes in the red cells were made by workers studying premature babies, although other authors played around the point.

As for the question of technic, I don't know whether Dr. Diamond really intended to imply that a reliable worker would get a 50 per cent variation in repeated red cell counts for the same subject. I dare say there are workers who get that variation, but I should not classify them as reliable. I have no fancy apparatus. I have nothing the clinician cannot use in his practice. In fact, I have been using for ten years all the implements I used when I was in practice; so there is no need for an explanation of any special technic. I am perfectly sure what my own errors are, since I have checked my results repeatedly every year, and if Dr. Diamond would like to know what the figures are I should be glad to show them to him.

So far as the reticulocyte count is concerned, I should mention, I think, that it presents the most difficulties from the technical standpoint. I have compared my work with that of Castle and with that of Sturgis, of Ann Arbor, Mich., and I know that they agree with me that greater errors in the reticulocyte counts are recorded in different regions than in any other single item in the blood count. I think it is important in interpreting hematologic figures to know who the technicians are. Unless one does know, such figures must be taken with a grain of salt.

REDUCTION OF SERUM REACTIONS

USE OF ANTITOXINS OF WHICH THE PROTEIN SPECIFICITY HAS BEEN ALTERED BY ENZYMIC DIGESTION

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In 1938 an opportunity arose to study the effects of new type diphtheria and scarlet fever antitoxins which, according to the manufacturer,[1] were so modified by a process of separating serum protein fractions that fewer serum reactions of all kinds could be expected with their use. These antitoxins were said to be "despeciated," a term indicating that their proteins were so altered that specific biologic reactions to horse serum were prevented when they were tested on laboratory animals. Specifically, it has been reported [2] that

> Digestion of antitoxic plasma or sera with the enzyme "Taka-diastase" yields a refined antitoxin which has lost so much of its horse-serum specificity that it can be injected into guinea pigs which have been sensitized to normal horse serum without the appearance of any serious anaphylactic symptoms.

Studies of the new antitoxins have indicated that the antitoxin molecule is altered only slightly, but that the alteration is enough to change its biologic specificity without impairing its antitoxic or antibacterial properties or potency.[3]

The results obtained with 61 patients who received "despeciated" diphtheria antitoxin and with 69 who were given "despeciated" scarlet fever antitoxin are the basis of this report. Before presenting the clinical data on these 130 patients the following case history of the first patient to receive the new type antitoxin is recounted, because of its interest and because it illustrates the type of case in which the advantages of the new antitoxins are best revealed.

From the Communicable Disease Service, Herman Kiefer Hospital, and the Detroit Department of Health.

1. The diphtheria and scarlet fever antitoxins referred to in this paper as "special" or "despeciated" were supplied by Parke, Davis & Co.

2. Coghill, R. D.; Fell, N.; Creighton, M., and Brown, G.: Elimination of Horse-Serum Specificity from Antitoxins, J. Immunol. **39**:207 (Sept.) 1940.

3. Fell, N.; Stern, K. G., and Coghill, R. D.: Physical-Chemical Study of Normal and Immune Horse Sera, J. Immunol. **39**:223 (Sept.) 1940.

REPORT OF A CASE

E. G., a girl aged 13 years, became ill on Jan. 26, 1938 and complained of the following symptoms: sore throat, headache, chills and fever. On February 1 the cervical glands were swollen and swallowing was painful, and the patient was admitted to Herman Kiefer Hospital in a critical condition. Examination revealed slight nasal discharge and a gray membrane on the tonsils, the uvula, the anterior faucial pillars and the posterior pharyngeal wall. Diphtheria antitoxin, 40,000 U. S. P. H. S. units, was described and the reaction to a cutaneous test consisting of the intracutaneous injection of 0.2 cc. of a 1:10 dilution of normal horse serum was read as positive. The cutaneous test was performed at 7:50 p. m., and by 8 p. m. the patient had severe urticaria and difficulty in breathing; so 5 minims (0.31 cc.) of epinephrine hydrochloride (1:1,000) was given hypodermically at once and another 5 minims at 8:10 p. m. One minim (0.06 cc.) of diphtheria antitoxin, diluted 1:20, was administered subcutaneously with 3 minims (0.18 cc.) of epinephrine hydrochloride at 8:45 p. m.; 2 minims (0.12 cc.) with 2 minims of epinephrine hydrochloride was given at 9:30 p. m., and at 10:15 p. m. 5 minims of antitoxin with 1 minim of epinephrnie was administered. Further desensitization was discontinued because of the marked urticaria and distress encountered. Throughout the night urticaria was troublesome. Sedation, applications of calamine lotion to the urticarial lesions and administrations of epinephrine were necessary. The following morning a cutaneous test was performed with a 1:20 dilution of diphtheria antitoxin. The reaction appeared to be negative after twenty minutes, but after 1 minim of the 1:20 dilution was given subcutaneously a reaction occurred.

The temperature on admission was 100.2 F., and the pulse rate 86 and the respiratory rate 20. The temperature did not rise during the period that serum sickness was present, but the pulse rate rose to 135, and the morning after admission the pulse rate was 120 and the temperature 100.6 F.; the urticaria had disappeared, and the only reaction noted was that following the subcutaneous injection of the 1:20 dilution of serum.

Inquiry was made concerning the availability of goat serum, and through Parke, Davis & Co. goat serum was made available for testing purposes, but it was discovered that there was an insufficient amount for therapeutic use. However, a concentrated experimental diphtheria antitoxin was available, and the reactions to cutaneous tests in which both goat serum and a 1:10 dilution of the concentrated experimental antitoxin were used proved negative. After the reading of these reactions it was decided to give the experimental serum in desensitizing doses at one-half hour intervals, beginning with 1 minim and doubling the dose at each subsequent injection. The first dose (1 minim) was given at 1 p. m. By 4 o'clock 2 cc. had been given intramuscularly, and at 5 o'clock the remainder of the 40,000 units was given intramuscularly. No untoward effects occurred as a result of using the experimental serum, and after its injection the patient's condition became progressively better.

On the sixth day in the hospital a few urticarial wheals were present on the abdomen and the arms, and 10 minims (0.65 cc.) of epinephrine hydrochloride was given at 9:45 in the morning. Slight urticaria was present on the seventh day but had disappeared by that evening. On the evening of the eighth day severe urticaria occurred over the entire body, beginning at 9 p. m. This persisted for three days. No urticaria or rise in temperature was observed after the eleventh day in the hospital. The patient had a serious form of diphtheria and was, therefore, kept in the hospital because of the possible occurrence of paralysis. A mild

form of myocarditis of the "B," late or low blood pressure type did develop, but she was dismissed, recovered, on the forty-second hospital day.

Because of the degree of sensitivity exhibited by this patient it would have been impossible to use ordinary antitoxin. The concentrated experimental antitoxin proved very satisfactory in this case, for there was no accelerated serum reaction after the injection of 40,000 units. Severe urticaria did develop at the usual time, but this complication can hardly be considered as hazardous to life and must be taken as an unpleasant side effect rather than as an important complication or a contraindication to the use of serum. A similar experience with the new type antitoxin has been reported by Schaeffer and Myers.[4]

RESULTS OF TREATMENT WITH NEW TYPE DIPHTHERIA ANTITOXIN

Sixty-one patients received antitoxin and were in the hospital nine days or longer (average, twenty-four and four-tenths days). Of these, 34 [5] had positive reactions to cutaneous tests with a 1:10 dilution of horse serum on admission. This high incidence was due to the method of selection. An attempt was made to include all patients with positive cutaneous reactions in the special group, so that the new product might be given a much severer test. The incidence of serum reactions among the 61 patients was 10 per cent. This fact is taken as evidence of "despeciation" of the antitoxin, for with our method of selecting patients a much higher incidence of allergic reactions would have been expected in this group than in that of Toomey and Kimball.[6]

The reactions of 2 of the 6 patients who had urticaria were mild, in that they lasted less than two days, were not associated with a rise of temperature and did not require treatment. The reactions of the remaining 4 patients were classed as moderate; none were severe. In the case of 1 patient with a moderate reaction urticaria appeared on the third day after serum was given, which constituted an accelerated reaction.

In addition to the 61 patients who made up the foregoing group, an additional 15 received the new antitoxin but were in the hospital less than nine days. These patients were sent into the hospital with a diagnosis of diphtheria, but they were subsequently proved to have other disorders, distributed as follows: acute tonsillitis, 6; septic sore throat, 3; pharyngitis, 2; scarlet fever, 2; laryngitis, 1, and secondary syphilis, 1. Of these 15 patients, 6 had positive reactions to cutaneous tests; all received

4. Schaeffer, M., and Myers, G. B.: Tetanus in a Serum-Sensitive Patient Successfully Treated with a New "Despeciated" Antiserum, J. Allergy **12**:188 (Jan.) 1941.

5. Eight of these had negative reactions to cutaneous tests with "despeciated" diphtheria antitoxin. However, no attempt was made to compare the incidence of positive reactions in tests done with the two types of antitoxin at the beginning of the study; so no conclusions can be drawn.

6. Toomey, J. A., and Kimball, E. R., Jr.: Treatment of Scarlet Fever with Specific Antitoxins of Low Protein Content, J. Pediat. **15**:238 (Aug.) 1939.

antitoxin, and only 1 had a serum reaction, which consisted of a light chill and fever after 40,000 units of antitoxin was given intravenously. No other reactions were observed, although it cannot be said whether some may not have had serum sickness after discharge from the hospital. The duration of stay in the hospital for the 15 patients was as follows: three days, 1; four days, 3; five days, 7; six days, 3, and seven days, 1.

No attempt is made in this report to evaluate the therapeutic effectiveness of the new type antitoxin. Other investigators have indicated that the therapeutic value of serums and antitoxins so treated is unchanged. Our observations do not conflict with this opinion. Of the 76 patients making up the special group, 3 died. These patients had been ill fourteen, seven and seven days respectively before admission to the hospital (and the beginning of treatment). All were recognized as being critically ill on admission, and each received 100,000 units of antitoxin, in part intravenously, in addition to the usual supportive therapy.

RESULTS OF TREATMENT WITH OLD TYPE DIPHTHERIA ANTITOXIN

The control group of 100 patients were treated with a refined and concentrated antitoxin similar to that in general use. These patients were selected by the alternate method, modified, as previously stated, by the decision to give all patients with a positive reaction to a cutaneous test the "despeciated" antitoxin. However, among the 100 control patients 3 with positive reactions to cutaneous tests were included, either because they chanced to arrive at the hospital when the "despeciated" antitoxin was not available or because they had had antitoxin before admission.

Among the control patients 18 per cent had serum sickness; and it is not known whether 1 or more of the 3 patients who stayed in the hospital less than ten days (2 remained only five days and 1 seven days) may have had serum sickness. Of the 18 instances of serum reaction 3 were classed as mild, 13 as moderate and 2 as severe.

In the control group there were 4 deaths; so the fatality rate for the patients given "despeciated" antitoxin and that for the control group were equal. Three of the control patients who died were classified as critically ill on admission and the fourth as very ill; 1 had been ill for only two days before admission, 1 for three days, 1 for five days and the fourth for six days.

In evaluating the incidence and the severity of serum sickness in this study one factor must be taken into consideration, that is, the routine use of pitressin (the pressor principle of the posterior lobe of the pituitary) at four hour intervals for all patients who showed any evidence of peripheral circulatory paralysis. Eight patients in the control group fell into this subgroup. None of the 8 had serum sickness. It is a

matter for speculation whether any serum reactions were prevented by pitressin. Four patients in the special group received pitressin, and none had serum sickness. It is our opinion that an incidental result of the routine use of pitressin in cases of impending or frank circulatory failure may be the prevention of serum sickness.

RESULTS OF TREATMENT WITH NEW TYPE SCARLET FEVER ANTITOXIN

Sixty-nine patients were treated with "despeciated" scarlet fever antitoxin. Of these, 40 had positive reactions to cutaneous tests with

*Incidence of Serum Reactions Among Patients Given "Despeciated" Antitoxin and Among Controls**

	Patients Given "Despeciated" Antitoxins		Controls (Patients Given Refined and Concentrated Diphtheria Antitoxin)
	Scarlet Fever	Diphtheria	
Total number	69	61	100
Number reacting positively to cutaneous test with 1:10 dilution of horse serum	48	34	3
Number showing immediate reactions	0	0	0
Number showing serum sickness	8 (4 mild, 2 moderate, 2 severe)	6 (2 mild, 4 moderate, 0 severe)	18 (3 mild, 13 moderate, 2 severe)
Expected percentage of reactions with old style antitoxin †	70+	55+	25-50
Actual percentage of serum reactions	10	10	18

* So far as possible, all patients who had a positive reaction to a cutaneous test were given "despeciated" antitoxin. Controls were patients admitted concurrently who had negative reactions to cutaneous tests. In all other respects these two groups were comparable and received the same treatment.

† The figures in the column "Expected percentage of reaction with old style antitoxin" for the special group are estimates based on the assumption that practically all persons who have a positive reaction to a cutaneous test will have some degree of allergic reaction when given old style antitoxin, and the range "25-50," for controls, is based on past experience and reports in the medical literature.

normal horse serum, 8 had questionable reactions, and 21 negative reactions. Here, again, the high incidence of positive reactions was due to the method of selecting the patients. It was at first planned to use the new type of antitoxin only for patients with positive reactions to cutaneous tests with horse serum. But as the study proceeded it became evident that "despeciated" antitoxin was much safer so far as allergic reactions were concerned, and it was administered to several patients whose reactions to cutaneous tests were negative.

The opinion of the admitting physician with regard to the severity of the patient's illness on admission was recorded as follows: Forty-nine patients were ill; 19 were very ill, and 1 was critically ill. All of the patients recovered.

All patients except 3, who had two therapeutic doses, received one therapeutic dose (9,000 U. S. P. H. units) of scarlet fever antitoxin.

Twenty-five received sulfanilamide, and 5 received a therapeutic dose of scarlet fever convalescent serum in addition to the antitoxin. Reference to therapy other than serum is mentioned, but it is not believed that the incidence of serum reactions was affected thereby.

Only 8 reactions, including serum sickness, occurred among the 69 patients. This seems remarkable, especially in view of the fact that 40 patients (58 per cent) had definitely positive reactions to cutaneous tests with horse serum and an additional 8 patients showed a questionable response to the test.

So far as could be judged by the results with this group, there was no reason to suspect that the process of digestion and "despeciation" to which the antitoxins were subjected in manufacture had altered their therapeutic value. Only 14 of the 69 patients remained in the hospital beyond the minimum isolation time required by law. Additional days in the hospital were due to the usual complications, such as suppurative otitis media and cervical adenitis, and, in 2 instances, to the fact that the patients were found to be diphtheria carriers.

COMMENT

Schaeffer and Myers [4] have reported the successful use of "despeciated tetanus antitoxin for a patient who, like the one reported on in detail earlier in this paper, was so sensitive to regular tetanus antitoxin that he could not be treated with it. They performed cutaneous tests on their patient one year later with 1 : 10 dilutions of both horse serum and "despeciated" antitoxin and found that he reacted positively to both. As serotherapy was not needed on the latter occasion, no information was obtained on an important point, namely, the response of patients to readministration of "despeciated" antitoxins.

Baird [7] gave "despeciated" scarlet fever antitoxin to 229 persons, of whom 54 were contacts and 175 had scarlet fever. Complete protection was obtained for the 54 contacts. There were 3 mild allergic reactions in this group. Of the 175 patients given "despeciated" antitoxin therapeutically, only 3 had serum reactions. Toomey and Kimball [6] treated over 500 patients with scarlet fever with "despeciated" antitoxin and observed a 10 per cent incidence of serum reactions. This figure included all reactions which could be attributed to serum therapy. In the experience of these clinicians, the process which brings about "despeciation" of antitoxin apparently does not result in loss of therapeutic effectiveness. Hutchison [8] has reported on a series of 300 patients given diphtheria antitoxin prepared by Pope's process ("enzyme disaggregation followed by differential heating"). No "serum rashes" were observed, and few

7. Baird, J. S., in discussion on Lucchesi, P. F.: Worthwhile Immunization Procedures, Pennsylvania M. J. **42**:524 (Feb.) 1939.

8. Hutchison, A.: Treatment of Diphtheria with Refined Antitoxin, Brit. M. J. **1**:384 (Feb. 25) 1939.

immediate reactions were encountered; those noted were mild and followed intravenous administration of antitoxin. Arlt,[9] using diphtheria antitoxin prepared by a similar process, encountered an incidence of serum reactions of only 3.9 per cent among 504 patients.

Our experience coincides with that of others who have used "despeciated" antitoxins in that we found a greatly reduced incidence of allergic reactions. The method of preparation used appears to be an advance in biologic therapy. The immediate advantages of "despeciated" serums are threefold: First, patients who are very sensitive to serums prepared in the usual way may now be treated effectively in most instances. Second, the incidence of serum reactions of all kinds can be greatly reduced. Third, it seems probable that serotherapy may now be used for certain patients to whom it was formerly denied. Many physicians hesitate to employ serotherapy in cases of moderately severe scarlet fever because they fear that sensitivity to horse serum may preclude the use of diphtheria or tetanus antitoxin later on. Whether or not "despeciated" antitoxins remove this bar to the more widespread use of serotherapy remains to be answered on the basis of additional clinical information, particularly with regard to the tolerance of patients to readministration of these antitoxins at intervals of a few months or years.

Published reports on clinical uses of the new antitoxins indicate that the incidence of reactions (allergic) of all types is under 10 per cent when a large number of consecutive, unselected patients are treated. This rate compares favorably with a control incidence of 40.5 per cent among 2,675 patients reported on by Fox[10] and that of 43.6 per cent among 87 controls given regular antitoxin by Toomey and Kimball.

CONCLUSIONS

The incidence of allergic reactions among 130 patients who were given a new type ("despeciated") antitoxin is reported. Serum reactions of all kinds were greatly reduced, and certain patients who could not tolerate regular (refined and concentrated) antitoxins were successfully treated with the new products.

The new type antitoxins are purified and concentrated by an enzymic process which is said to eliminate a large proportion of the serum protein and to change the remaining proteins so that the original horse serum specificity is greatly reduced. However, as with all biologic preparations of horse serum, the usual precautions should be observed, especially with patients known to be sensitive to horse serum or horse dander.

Availability of less reactive, "despeciated" antitoxins and antiserums should extend somewhat the field of serotherapy.

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9. Arlt, H. G.: Diphtherie-Fermoserum, München. med. Wchnschr. **87**:696 (June 28) 1940.

10. Fox, M. J.: Relation of Incidence of Human and Animal Serum Disease, J. Infect. Dis. **61**:341 (Nov.-Dec.) 1937.

CEREBRAL ABSCESS AND PARADOXIC EMBOLISM ASSOCIATED WITH CONGENITAL HEART DISEASE

REPORT OF SEVEN CASES, WITH A REVIEW OF THE LITERATURE

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Of the 25,620 autopsies performed during the past twenty-one and a half years by the department of pathology of the Los Angeles County Hospital, in 160 congenital defects of the heart and the great vessels were observed; thus in this large series the percentage incidence was 0.62 as compared with that of 1.29 for the series of 75 cases at Johns Hopkins reported by Leech [1] and that of 5.24 for the 1,950 autopsies conducted at Children's Memorial Hospital, Chicago, reported by Gibson and Clinton.[2] Of these 160 cases, there was a paradoxic embolism in 1 and cerebral abscess was present in 6. In 4 of the 7 cases the intracranial complication was suspected before death.

The literature has been reviewed to January 1941, and the pertinent data have been tabulated and discussed.

REPORT OF CASES

CASE 1.—M. B., an 18 year old girl, had had an attack of sneezing three days before admission and had had diplopia for three days, frontal headache for two days and lumbar backache for one day prior to admission. Weakness of the right arm and leg developed a few hours after the backache. The patient had had palpitations for several years.

Physical Examination.—On admission the temperature was 101 F., the pulse rate 108, the respiratory rate 20 and the blood pressure 120 mm. of mercury systolic and 96 mm. diastolic. She was stuporous and had paresis of the right side of the face, with unequal, irregular, fixed pupils. Left internal strabismus was present, and the uvula deviated to the right, with absence of the gag reflex. There was moderate nuchal rigidity, and Kernig and Brudzinski signs and a Babinski sign on the right were present. The deep reflexes were variable. Examination of the heart, lungs and abdomen showed no abnormalities.

From the Department of Pathology, Los Angeles County Hospital.

1. Leech, C. B.: J. Pediat. **7**:808, 1935.

2. Gibson, S., and Clifton, W. M.: Congenital Heart Disease: Clinical and Post-Mortem Study of One Hundred and Five Cases, Am. J. Dis. Child. **55**:761 (April) 1938.

Examinations of Spinal Fluid.—On admission the cerebrospinal fluid was clear and under a pressure of 200 mm. of water, and there were 56 cells per cubic millimeter, mostly polymorphonuclears. Eight drops of spinal fluid reduced 5 cc. of Benedict's solution, and the Pandy test showed a trace of globulin. The protein content was 136 mg. per hundred cubic centimeters. The Wassermann reaction was negative.

On the third day in the hospital the spinal fluid was grossly cloudy and contained 1,056 cells, mostly polymorphonuclears, and many staphylococci. A culture was sterile. There were 680 mg. of chlorides per hundred cubic centimeters, a reduced sugar content and a 4 plus reaction to the Pandy test. The Wassermann reaction was negative. The pressure was not recorded.

Course.—The patient became progressively more stuporous; difficulty in breathing developed, and she died on the third day in the hospital, at which time a systolic apical murmur was first heard.

Postmortem Examination.—The meninges were markedly injected, and there was a small amount of exudate over the pia mater. The brain appeared edematous. After fixation, sectioning of the brain revealed discoloration of the internal capsule with softening and destruction of the thalamus on the left by a poorly encapsulated abscess. Free pus was found in the lateral ventricle. Microscopic examination of the edge of the abscess showed early connective tissue proliferation.

Simple ovarian cysts were also present. Mesenteric adenitis was observed, but no evidence of infection was found elsewhere. The right side of the heart showed slight hypertrophy and opening the heart revealed basal intraventricular septal defect measuring 2 cm. There was thickening of the edge of the mitral valve, but no vegetations were present.

Cultures of material from the abscess yielded no growth, and a streptococcus was removed from the culture of a fecal specimen taken at autopsy.

CASE 2.—Two weeks before admission S. L. S., a 34 year old woman, experienced a sudden headache; she had never had one previously. It became progressively worse, and stiffness of the neck appeared a week later, but she did not present herself at the hospital for another week.

Physical Examination.—There was questionable enlargement of the heart, with occasional extrasystoles and a blowing diastolic murmur, heard at Erb's point. The blood pressure was 130 mm. of mercury systolic and 80 mm. diastolic. There were marked edema of the ankles and bilateral knee clonus. On admission the temperature was 101 F., the pulse rate 100 and the respiratory rate 22.

Laboratory Data.—A blood culture was sterile. The spinal fluid on admission was under a pressure of 75 mm. of water. There were 1,500 cells per cubic millimeter, with 80 per cent polymorphonuclears, and a negative reaction to the Pandy test. There were 680 mg. of chlorides and 37 mg. of sugar per hundred cubic centimeters. Culture yielded no growth. On the second day in the hospital the pressure was 130 mm. of water, the cell count was 1,260 and a culture was sterile. Culture and examination of two other specimens of spinal fluid gave similar results.

Course.—The course was septic, with lethargy, which became stupor, development of conjugate deviation of the eyes to the right, increase in the deep reflexes and marked ankle clonus. Death occurred in six days.

Postmortem Examination.—There were slight enlargement of the heart and hypertrophy of the right ventricle. Section revealed a basal intraventricular septal defect measuring 2 cm. which had a flaplike valve.

The meninges and the cortical vessels were injected and edematous and were covered by a purulent exudate. After fixation a well defined abscess measuring 3 cm. was discovered in the left frontal lobe; it had ruptured into the anterior horn of the left lateral ventricle. Smears and culture of the pus revealed Haemophilus influenzae.

CASE 3.—At birth the patient, a 10 year old girl, was a blue baby, and she had had occasional attacks of cyanosis. She had had a headache for four days and had gradually become stuporous.

Physical Examination.—The temperature was 99.6 F., the pulse rate 104 and the respiratory rate 26. The patient was stuporous and cyanotic and showed

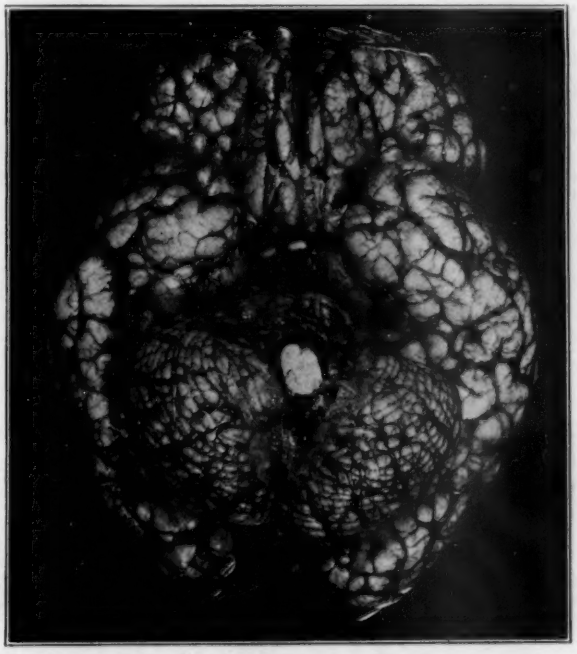

Fig. 1 (case 3).—Brain, showing basilar meningitis.

marked clubbing of the fingers and toes. She was emaciated and smaller than the average for her stated age. There were weakness of the right side of the face, a stiff neck, hyperactive knee jerk on the right side, bilateral ankle clonus and Babinski, Gordon, Chaddock and Oppenheim signs on the right. Kernig and Brudzinski signs were present. The apex beat was heard 1 cm. lateral to the clavicular line. There was an apical shock with harsh, diffuse, precordial murmur with diffuse transmission but with a maximal intensity at the left sternal border in the fourth interspace.

Examination of Spinal Fluid.—The spinal fluid was under a pressure of 300 mm. of water; there were 89 cells per cubic millimeter, mostly lymphocytes, sugar was absent and the globulin content was normal. A culture was sterile and the Wassermann reaction was negative.

Course.—The patient became comatose, the temperature rose to 104 F. and she died within thirty-six hours.

Postmortem Examination.—There were moderate enlargement and dilatation of the right side of the heart. The cusps of the pulmonary valve were fused to form a membrane which practically occluded the narrowed pulmonary orifice, which was 1 cm. in diameter, and there were several vegetations on the edge of the valve. The cusps of the tricuspid valve were thickened, and the chordae tendineae were shortened; there were some pinpoint vegetations on the free edge of the valve. There was a basal intraventricular septal defect measuring 2.5 cm., over which the aorta originated. The foramen ovale was patent but

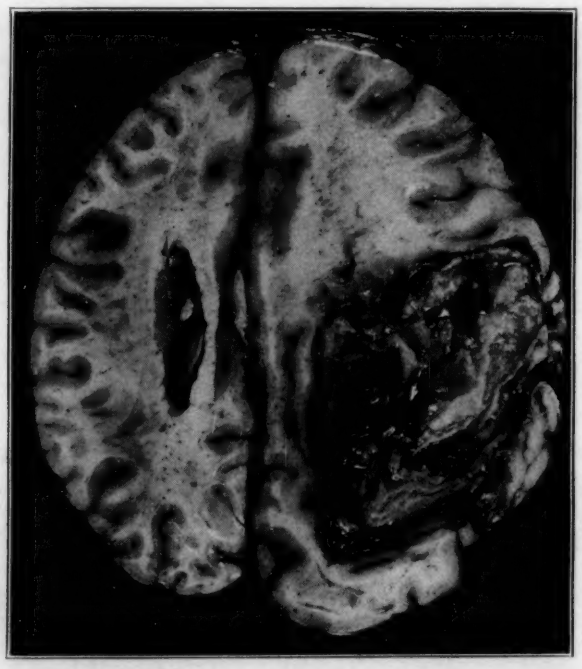

Fig. 2 (case 4).—Section of brain, showing abscess in right temporal region.

did not communicate with an intra-auricular septal defect in the lower and posterior portion of the auricular septum.

The vessels of the pia mater were engorged; the base of the brain was covered by pus. The ventricles were dilated. There was an area of hemorrhagic softening in the left side of the thalamus, and a red infarct was present posterior to it. The histologic picture was that of a peripheral round cell infiltration and central necrosis, resembling early abscess formation. From the pus at the base of the brain H. influenzae was cultured.

CASE 4.—At birth A. L. F., a 3 year old boy, had been a blue baby, but he had been in good health until three days prior to admission, when weakness of the left leg, which caused him to limp, was noted. The next morning the left leg and arm were paralyzed.

Physical Examination.—The temperature was 100 F., the pulse rate 110 and the respiratory rate 24. The patient was markedly cyanotic. The tonsils were enlarged but not grossly infected. There were a diffuse precordial thrill and a systolic murmur with maximum intensity at the pulmonic area. There was also a loud, low-pitched systolic murmur at the base, with diffuse transmission. The liver was 2 fingerbreadths below the costal margin. There was marked clubbing of the fingers and toes.

Laboratory Data.—The blood had a hemoglobin content (Sahli) of 102 per cent. The white cell count was 15,000, with 68 per cent polymorphonuclears. The urine was normal except for the presence of 5 to 6 white blood cells per high power field; culture yielded Staphylococcus aureus. The spinal fluid was under a pressure of 100 mm. of water, there were 9 cells per cubic millimeter and 670 mg. of chlorides and 14 mg. of protein per hundred cubic centimeters. The Wassermann reaction was negative, and a culture was sterile, as were four blood cultures.

Course.—The illness lasted over ten days, with low grade fever and a terminal rise in rectal temperature to 103 F., but at no time were there any meningeal signs. Before death the paralyzed extremities became spastic and the patient became first irritable and then stuporous.

Postmortem Examination.—The meninges contained petechiae. The gyri were flattened over the right temporal lobe and the sulci narrowed; the area was fluctuant. Section and dissection did not reveal an embolus, but an egg-sized, irregular, walled cavity filled with pus was present under the area of fluctuation. There was hypertrophy of the right side of the heart. The pulmonary artery was 3 mm. in diameter and had a sclerosed, thickened valve formed by two cusps. There was a basal intraventricular septal defect measuring 2.5 cm., over which the aorta originated. There were no vegetations in the heart.

CASE 5.—L. L., a 19 year old boy, had been constantly cyanotic since birth and had experienced dyspnea on exertion. One week prior to admission he had had a sore throat and a right earache, with a throbbing headache. The next day blurring of the vision developed.

Physical Examination.—The temperature was 99 F., the pulse rate 100 and the respiratory rate 24; the systolic blood pressure was 110 mm. of mercury and the diastolic pressure 72 mm. Pulsations of the vessels in the neck, clubbing of the fingers and toes and swelling of the right inferior turbinate were noted. The heart was enlarged, and there was a hard, harsh systolic murmur with a thrill, of which the point of maximal intensity was in the fourth left intercostal space at the lateral sternal border. The murmur completely obscured the heart sounds. The deep reflexes were all hyperactive, with bilateral ankle clonus. Kernig and Brudzinski signs were present. Examination of the fundi showed blurring of the disk of the optic nerve.

Laboratory Data.—On admission the spinal fluid was under a pressure of 80 mm. of water; examination showed 96 cells per cubic millimeter, with 66 per cent polymorphonuclears, a 1 plus reaction to the Pandy test and 670 mg. of chlorides per hundred cubic centimeters. Ten additional examinations showed cell counts varying from 890 to 14,000, with from 65 to 100 per cent polymorphonuclears, Pandy reactions ranging from 2 plus to 4 plus, and chlorides varying in amount from 680 to 700 mg. per hundred cubic centimeters. Two blood cultures were sterile. The Wassermann reactions of the blood and spinal fluid were negative.

Course.—The patient had low grade, septic fever with increasing meningeal signs, stupor and, finally, coma and death occurred on the sixteenth day.

Postmortem Examination.—Pus was found in the sphenoid sinus and the ethmoid cells. Gray-green pus was present along the intracranial vessels and along the injected meninges and the pial vessels. There was a well encapsulated abscess measuring 3.5 by 2.3 cm. in the right occipital lobe and extending into the posterior horn of the lateral ventricle. The heart was enlarged and dilated, and the right side was hypertrophied. The subpulmonic area showed marked stenosis, and the pulmonary artery, though patent, was only 4 mm. in diameter. There was a

Fig. 3 (case 5).—Section of brain, showing well encapsulated abscess in right occipital lobe.

funnel-like defect involving the midportion of the muscular part of the intraventricular septum, with the narrower orifice opening into the right ventricle.

CASE 6.—The patient, a woman aged 46, had had a pain in her knee and fever for one week and a rash for three days before admission.

Examination.—On admission the patient, who was obese, was comatose, febrile and cyanotic. Petechiae were present on the skin and the mucous membranes, and there was a rough, apical systolic thrill. The blood pressure was 94 mm. of mercury systolic and 54 mm. diastolic. Blood culture yielded no growth.

Course.—The patient became unconscious and died in ten hours. Hyperpyrexia (temperature, 105 F.) developed, but no definite signs of intracranial involvement were observed.

Postmortem Examination.—The coroner reported that there were multiple areas of softening with petechial hemorrhages in the cortex of the right frontal lobe. The only abnormality in the heart was the presence of an intra-auricular septal defect measuring 4 cm. at the location of the foramen ovale.

Microscopic examination (performed by the department of neuropathology of the Los Angeles County Hospital) showed small red infarcts containing many small abscesses in the right frontal lobe.

CASE 7.—The patient, a 70 year old woman, had been an outpatient for thirteen years, during which time she had had immature cataracts. Two days prior to admission she fell and injured her right knee, hip and shoulder, after which she was unable to walk.

Physical Examination.—On admission the temperature was 100.4 F., the pulse rate 120, the respiratory rate 24 and the blood pressure 200 mm. systolic and 100 mm. diastolic. There was slight cardiac enlargement. The first tone was roughened and loud at the apex; the aortic second sound was more pronounced than the pulmonic second sound. There was tenderness of the right shoulder, and the right knee showed discoloration and pain on motion. A roentgenogram showed a comminuted fracture through the medial condyle.

Course.—The patient was discharged to a rest home, and thirteen days later she returned to the hospital, comatose and with deviation of the eyes to the right, paralysis of the right arm and the right side of the face, pinpoint pupils and a bilateral Babinski sign. The left arm was cold, but good pulsation was present in both dorsalis pedis arteries. She died thirteen hours after admission.

Postmortem Examination.—There was a large embolus in the left internal carotid artery and its midcerebral branch. A white fibrin clot measuring 2 cm. was present in the right ventricle, and a patent foramen ovale 1.5 cm. in diameter and a calcified aortic ring were observed. Emboli were also found in the left subclavian and the superior mesenteric arteries and in the major branches of the pulmonary arteries. There were an organizing thrombus in the right popliteal vein and a fracture of the right tibia. Moderate arteriosclerosis was also present.

COMMENT

Paradoxic Embolism.—Probably the first case of paradoxic embolism described was that reported by Cohn [3] in 1860, but it remained for Cohnheim [4] to trace the course of such an embolus from a venous thrombosis through a patent foramen ovale to the arterial circulation. Numerous reports have appeared since, and to date 35 cases have been reported, excluding the case of Buhlig [5] and including that of Louis, cited by Ballet.[6] Since no previous bibliography has been complete, the reported cases have been listed in chronologic order in table 1.

3. Cohn, B.: Klinik der embolischen Gefässkkrankheiten, Berlin, A. Hirschwald, 1860; cited by Hirschboeck (Am. J. M. Sc. **189**:236, 1935), Abbott, Lewis and Beattie (Am. J. M. Sc. **165**:636, 1923) and Ingham.[12b]

4. Cohnheim, J.: Vorlesungen über allgemeine Pathologie, Berlin, A. Hirschwald, 1877, vol. 1, p. 131; cited by Abbott, Lewis and Beattie (Am. J. M. Sc. **165**:636, 1923) and Ingham.[12b]

5. Buhlig, W. H.: Am. J. M. Sc. **128**:992, 1904.

6. Ballet, G.: Arch. gén. de méd. **5**:659, 1880; cited by Rabinowitz, Weinstein and Marcus.[14]

A greater number of the patients were females than males, and the ages varied from 1½ to 70 years. In a majority of the cases the embolism occurred after the age of 50 years.

No cause for the formation of a thrombus, a part of which might act as an embolus, was found in about one half of the cases reviewed. In 13 cases the disease occurred in from three days to two and a half weeks after an operation. In case 7 of the present report embolism occurred two and a half weeks after the fracture of a tibia, and in another case [7] the embolism occurred six weeks post partum. In approximately half the cases autopsy showed thrombosis of the veins of the lower extremities and the pelvis, including the hemorrhoidal vein.[8] In 3 cases [9] an antemortem

TABLE 1.—*Chronologic Listing of Reported Cases of Paradoxic Embolism* *

Author	Year	No. of Cases
Cohn [3]	1860	1
Cohnheim [4]	1877	1
Louis, cited by Ballet [6]	....	1
Zahn: Rev. méd. de la Suisse **1**: 227, 1881	1881	1
Rostan: Thesis, Geneva, 1884	1884	3
Hauser: München. med. Wchnschr. **35**: 583, 1888	1888	1
Ohm: Ztschr. f. klin. Med. **61**: 374, 1907	1907	1
Beattie: Internat. A. M. Museums Bull. **11**: 64, 1925	1925	2
Versé: Verhandl. d. deutsch. path. Gesellsch. **13**: 215, 1930	1930	2
Bernard: Quart. J. Med. **23**: 305, 1930	1930	1
Thompson and Evans: Quart. J. Med. **23**: 135, 1930	1930	7
French: Arch. Path. **11**: 383, 1931	1931	1
Taylor: Arch. Path. **16**: 901, 1933	1933	1
Armand-Delille and Lesobre: Bull. Soc. de pédiat. de Paris **33**: 274, 1935	1935	1
Hirschboeck: Am. J. M. Sc. **189**: 236, 1935	1935	1
Neely: Nebraska M. J. **21**: 61, 1936	1936	1
Jones: Brit. M. J. **2**: 225, 1936	1936	1
Koritschoner: J. A. M. A. **106**: 1269, 1936	1936	1
Ingham: Am. J. M. Sc. **196**: 201, 1938	1938	7
Hanna	1941	1

* The case of Buhlig,[5] reported in 1904, is not included.

interauricular thrombus served as a focus, and in the remaining cases the site of the focus either was not reported or was not discovered.

In the majority of the cases infarcts were multiple; the emboli which caused death occurred most frequently in the pulmonary and the cerebral circulation, but more rarely they lodged in the bifurcation of the aorta and in the superior mesenteric,[4] subclavian, innominate and carotid arteries.[10]

In most cases the congenital cardiac malformation which allowed the shunting of emboli from the venous to the arterial circulation was a

7. Thompson, T., and Evans, W.: Quart. J. Med. **23**:135, 1930.

8. Ohm, J.: Ztschr. f. klin. Med. **61**:374, 1907.

9. (*a*) Rostan, A.: Contribution à l'étude de l'embolie croisée consécutive à la persistance du trou de Botal, Thesis, Geneva, 1884. (*b*) Hauser, G.: München. med. Wchnschr. **35**:583, 1888. (*c*) Hanna, case 7.

10. Thompson and Evans.[7] Hanna, case 7. Cohn.[3]

patent foramen ovale. Intraventricular septal defects, with or without other anomalies, were infrequent.[11] In about 20 per cent of the cases the foramen ovale was occluded by an embolus which extended into both auricles and in 1 case into the left ventricle.[12]

The clinical course and symptomatology varied with the localization of the resultant infarction. Patients with massive occlusions of the pulmonary arteries and those with infarction of vital brain centers died early [13]; 1 patient survived the first infarct and died of a subsequent one.[7]

Ingham's case 7 [12b] is of special interest because it is the only one in the literature in which there were a brain abscess and an embolus of a pulmonary artery. Case 7 of Thompson and Evans [7] also is of interest, because it is the only report of intracardiac metastasis of a neoplasm and undoubted paradoxic embolism of tumor tissue from a malignant teratoma of the testicle.

Brain Abscess.—Including the cases in this report, 23 cases of formation of a brain abscess as a fatal event in association with congenital heart disease have been reported.

The average age at death was 19 years, the youngest patient being 3 and the oldest 57 years old; about one-half the patients were in the teens. In the 10 cases reviewed by Rabinowitz, Weinstein and Marcus [14] the average age of the patients was 16½ years. Case 4 of this report and the case of Farre [15] are the only ones in which the patient was 10 years of age.

The sex distribution shows a predominance of males, with a ratio of 13 :10.

The signs and symptoms are variable, depending on the type of congenital cardiac defect and the location and duration of the intracranial lesion. The most common cardiac lesions were: tetralogy of Fallot, 11 cases; patent foramen ovale, 6 cases; basal intraventricular septal defect without other abnormalities, 4 cases; basal intraventricular septal defect and patent foramen ovale, 1 case, and Eisenmenger complex,

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11. Armand-Delille, P. F., and Lesobre, R.: Bull. Soc. de pédiat. de Paris **33**:274, 1935. Louis, cited by Ballet.[6]

12. (*a*) French, L. R.: Paradoxical Embolism, Arch. Path. **11**:383 (March) 1931. (*b*) Ingham, D. W.: Am. J. M. Sc. **196**:201, 1938. (*c*) Rostan.[9a] Thompson and Evans.[7]

13. (*a*) Bernard, W. G.: Quart. J. Med. **23**:305, 1930. (*b*) Koritschoner, R. J.: Paradoxical Embolism, J. A. M. A. **106**:1269 (April 11) 1936.

14. Rabinowitz, M. A.; Weinstein, J., and Marcus, D.: Am. Heart J. **7**:790, 1932.

15. Farre, J. R.: Pathological Researches: On Malformations of the Human Heart, London, Longman [and others], 1814, Observation 3, pp. 24-25; cited by Rabinowitz, Weinstein and Marcus.[14]

TABLE 2.—*Data from Twenty-Three Reported Cases of Brain Abscess Associated with Congenital Heart Disease* *

Author	Year	Age of Patient, Years	Sex of Patient	Symptoms and Duration	Signs and Duration	Lesions of Heart and Brain	Pathologic Conditions
Farre [15]	1814	9	Male	Headache and fever, 4 days; cyanosis, 2 days	Left hemiplegia	Tetralogy of Fallot	Abscess in right cerebral hemisphere
Lelmand, cited by Ballet [6].....	1821	57	Female	Cyanosis and dyspnea, throughout life	Left hemiplegia	Patent foramen ovale; pulmonary stenosis; hypertrophy of right side of heart	Abscess in right frontal lobe; purulent meningitis
Berthody: M. Examiner, Philadelphia **1**: 261, 1845	1845	21	Female	Cyanosis and dyspnea, throughout life; headache, delirium, fever and coma	.....	Tetralogy of Fallot	Abscess size of pigeon egg in left occipital lobe; rupture into ventricle
Stone: St. Thomas Hosp. Rep. **56**: 811, 1881	1881	19	Female	Cyanosis and dyspnea, throughout life; sudden headache, with delirium, fever and coma	.....	Tetralogy of Fallot; endocarditis	Abscess in right occipital lobe; rupture into ventricle; purulent meningitis
Ballet [6] †	1880	15	Male	.....	Left hemiplegia, 10 days	Ventricular septal defect; malposed septum; aplastic right ventricle; both auricles emptied into left ventricle	Abscess in right frontal lobe; rupture into ventricle; purulent meningitis
Deneke: Arch. f. klin. Med. **89**: 39, 1906	1906	18	Male	Cyanosis, dyspnea and headache, 10 days	Left hemiplegia	Tetralogy of Fallot; patent ductus arteriosus	Abscess size of walnut in right cerebral lobe; a streptococcus recovered from pus
Abbott, Lewis and Beattie: Am. J. M. Sc. **165**: 636, 1923	1923	..	.....	Cyanosis, clubbing, dyspnea, convulsions and headache, 10 days	Right hemiplegia	Tetralogy of Fallot	Abscess in left frontal lobe; purulent meningitis; appendectomy 8 days after onset
Raab and others: Wien. Arch. f. inn. Med. **7**: 367, 1923	1923	15	Male	Cyanosis and dyspnea, 9 years; sudden headache and fever, 3 weeks	Left hemiplegia	Tetralogy of Fallot; patent foramen ovale	Abscess size of hen's egg in right cerebral hemisphere; rupture into ventricle; purulent meningitis
Bach:‡ Lancet **1**: 1009, 1928.....	1928	30	Male	Dyspnea and cyanosis, throughout life; frontal and temporal headache, 9 days; fever and coma, 1 day	.....	Tetralogy of Fallot; patent foramen ovale	Abscess in right temporal lobe; meningitis
Baumgartner and Abbott: Am. J. M. Sc. **177**: 639, 1929	1929	20	Male	Dyspnea and cyanosis, throughout life; headache, 2 weeks; drowsiness, difficult speech and coma	Left hemiplegia, bilateral choked disks	Eisenmenger complex	Abscess in right frontal, parietal and capsular regions; streptococcus recovered from pus
Evans: Lancet **1**: 131 and 1289, 1931	1931	50	Male	.....	.....	Patent foramen ovale	Abscess in right occipital lobe, 6 cm.
		41	Male	.....	.....	Patent foramen ovale	Abscess in left parietal lobe, 6 cm.
		17	Female	.....	.....	Patent foramen ovale, intraventricular septal defect	Abscess in right occipital lobe, 2 cm. in diameter

Rabinowitz, Weinstein and Marcus [14]	1932	14	Female	Headache, vomiting, malaise and fever, 1 week	Cyanosis, papilledema and polycythemia	Patent foramen ovale; tetralogy of Fallot	Abscess size of walnut in cerebellum; Escherichia coli recovered from pus
Ingham [12b]	1938	39	Female	Numbness of right side of face and right hand; twitching and swelling of right arm; infection of upper respiratory tract, 4 days	Polycythemia	Patent foramen ovale, pulmonary embolus	Abscess in left cerebral hemisphere
Wechsler and Kaplan: Arch. Int. Med. 66: 1282, 1940. Case 1...	1940	14	Male	Convulsions; headache on right side; numbness on left side and drowsiness, 2 weeks	Cyanosis, clubbing, exophthalmos, papilledema, palsy left side of face, hemiplegia, polycythemia	.....	Abscess in right frontal lobe; meningitis
Case 2§..	....	11	Female	Headache on right side, 3 days; convulsion of left leg; weakness of left arm and leg; infection of upper respiratory tract	Weakness of left side of face, spasticity of left leg and left hemiplegia	.....	Abscess in right frontal lobe; meningitis
Hanna: Case 1	1941	18	Female	Headache and diplopia, 3 days; backache, 2 days; weakness of right arm and leg and stupor, 1 day	Palsy of right side of face and papillary and meningeal signs	Basal intraventricular septal defect	Abscess in left side of internal capsule and thalamus; ventriculitis; meningitis
Case 2	....	34	Female	Sudden headache, 2 weeks; stiff neck, 1 week; stupor	Conjugate deviation to right; hyperactive deep reflexes	Basal intraventricular septal defect	Abscess in left frontal lobe; rupture into ventricle; H. influenzae recovered from pus
Case 3	....	10	Male	Frequent attacks of cyanosis and headache, 4 days fever	Cyanosis, clubbing and weakness of right side of face, with rigid neck and ankle clonus	Tetralogy of Fallot; patent foramen ovale; intra-auricular septal defect; endocarditis	Abscess in left side of thalamus with infarction; H. influenzae recovered from pus; meningitis
Case 4§	....	3	Male	Clubbing, cyanosis and weakness, 3 days; paralysis of left arm and leg, 2 days; fever	Left spastic hemiplegia, 12 days	Tetralogy of Fallot; bicuspid valve of pulmonary artery	Abscess size of egg in right temporal lobe
Case 5	....	19	Male	Sore throat and earache, 2 weeks; headache, 6 days; sore neck, 4 days; fever	Meningeal signs; blurred fundi, 12 days	Intraventricular septal defect	Abscess in right occipital lobe; rupture into ventricle; sterile pus
Case 6	....	46	Female	Coma, pain in knee, rash and fever	Cyanosis	Patent foramen ovale	Multiple small infected infarcts

* The cases are listed chronologically.
† There was no history of heart disease.
‡ There were dental extractions fourteen days before death.
§ The patient was a blue baby.

1 case. In 2 cases the exact nature of the cardiac lesion was not known. Those patients with small septal defects without other cardiac abnormalities appear to live longer than those with larger defects.

Fourteen abscesses were located in the right cerebral hemisphere, 8 in the left cerebral hemisphere and 1 in the cerebellum. Three of the lesions in the right hemisphere and 1 in the left were not localized; 5 occurred in the right and 2 in the left frontal lobe, 2 were in the right and 1 in the left temporal lobe, and 3 were located in the right and 2 in the left occipital lobe. Two lesions occurred in the left side of the thalamus, and in 1 case the lesions were multiple.

The exact pathogenesis remains unknown, but previous writers have expressed the belief that abscess formation is secondary to paradoxic embolism and that the embolus may be infected or, more commonly, that the infarcted area is infected after the vascular accident has occurred. Cases 3 and 6 of this report favor the second theory of pathogenesis, as in 1 case numerous small abscesses were found in the area of infarction, whereas in the other round cell infiltration and increased spotty areas of necrosis, an even earlier form of abscess formation, were present. If this second theory is correct, there must then be at least a temporary period of bacteremia, which was not established by blood culture in 3 of my cases after the onset of abscess symptoms. The procedure of making routine blood cultures for all pediatric patients with congenital heart disease has not yielded any evidence of temporary bacteremia. The fact that in my cases 1, 4 and 5, as well as in some of the previously reported cases, the abscesses were sterile is not significant, save to show that the host had overcome the actual infection. The organism most frequently present in the abscesses are H. influenzae and the beta hemolytic streptococcus.

The predominance of lesions in the right hemisphere may have an anatomic explanation. The innominate artery arises just at the arch of the aorta, and the blood reaching it is at the head of each pulsation; so small foreign particles could be more easily forced into this arterial trunk.

In approximately one half of the cases meningitis due to rupture of the abscess into the ventricular system was present. Since it is a common mistake to diagnose the meningitis rather than the ruptured abscess, I feel that it should be emphasized that abscesses not infrequently rupture and thereby cause meningitis.

The cases of Stone [16] and Raab and co-workers,[17] in which there was endocarditis, Bach's [18] case, in which there were dental extractions,

16. Stone, W. H.: St. Thomas Hosp. Rep. **56**:811, 1881; cited by Rabinowitz, Weinstein and Marcus.[14]

17. Raab, W., and others: Wien. Arch. f. inn. Med. **7**:367, 1923; cited by Rabinowitz, Weinstein and Marcus.[14]

18. Bach, F.: Lancet **1**:1009, 1928.

Ingham's [12b] case 7, case 2 of Wechsler and Kaplan [19] and my case 3, in which there was endocarditis and case 5, in which there was an infection of the upper respiratory tract, deserve special mention. A focus for the infectious agent may have been present in all these cases, but no evidence other than a coincident relation between the infections and the abscess exists. In the 2 cases of Wechsler and Kaplan and in Ingham's case 7 surgical drainage of the abscess was employed. This procedure may offer some hope for therapy, despite the fact that all 3 patients died several weeks after operation, as a result of the infection (meningitis) and not of the surgical intervention.

SUMMARY AND CONCLUSIONS

Paradoxic emboli occur most frequently in middle-aged persons, whereas paradoxic embolism with cerebral abscess formation is most frequently observed in patients in the teens. The series which have been reported are too small to allow significance to be attached to the sex distribution.

The production of embolism of this type requires shunting of blood bearing emboli from the right side to the left side of the heart through a defect of the septum that normally separates the venous and the arterial circulation. A patent foramen ovale was the most outstanding means by which shunting occurred in the cases of embolism alone, while the tetralogy of Fallot was most frequent in the cases in which abscesses were present. In several cases foci were found in venous thromboses, some of which occurred postoperatively, but in the majority no focus was demonstrable.

Two theories for cerebral abscess formation are offered, and 2 cases which demonstrate the second theory, that is, infection occurring after infarction, are discussed.

An attempt is made to explain the increased incidence of cerebral abscesses on the right side, and the comment is made that such abscesses tend to rupture into the ventricular system and produce meningitis, which is diagnosed, while the true pathologic condition is overlooked. Any patient with congenital heart disease and signs of infection of the central nervous system should be suspected of having a ruptured cerebral abscess. At times it is possible to localize such lesions.

The paucity of the literature on these two conditions is due only in part to their rarity; it probably results in part from the fact that in some cases the correct diagnosis has not been made.

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19. Wechsler, I. S., and Kaplan, A.: Cerebral Abscess (Paradoxic) Accompanying Congenital Heart Disease: Report of Two Cases, Arch. Int. Med. **66:** 1282 (Dec.) 1940.

MAGNESIUM NEEDS OF PRESCHOOL CHILDREN

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The paucity of data concerning the magnesium needs of man at different periods of his development has stimulated further study of magnesium retentions in children. The first report [1] from this laboratory, which included a review of the literature, was concerned primarily with a series of single ten day balance studies with individual children. Calcium and phosphorus retentions also were studied in order to determine if there are any interdependent relations among these three metabolites.

The present report represents part of a nine month study of the growth, osseous development and mineral metabolism of 3 preschool boys aged 4 years 10½ months, 4 years 9 months and 3 years 3 months, respectively, at the beginning of the study and considers the magnesium retentions at three levels of ingestion, any one of which might occur in a seemingly well selected diet. Data pertaining to the calcium, phosphorus and nitrogen retentions and to the physical development of the children, as well as to the general plan of the investigation, have already been reported in THE AMERICAN JOURNAL OF DISEASES OF CHILDREN.[2]

With the possible exception of magnesium at the lowest level of ingestion, the diets, which were constant from period to period, were believed to be adequate throughout the study. The modifications in the magnesium intakes were made chiefly by changing from a whole grain breakfast cereal and commercial whole wheat bread, supplying from 11.3 to 12.6 per cent of the total calories (period 1, table), to a refined breakfast cereal and white bread in one series of tests (period 2) and by decreasing the amount of egg and meat in a second series with refined breakfast cereal and white bread (period 3). In the third period 12.3 to 14.0 per cent of the total calories was supplied by cereal foods. Only distilled water was used for cooking and drinking; thus the magnesium ingested came from food alone.

From the Iowa Child Welfare Research Station, State University of Iowa.

1. Daniels, A. L., and Everson, G. J.: A Study of the Magnesium Needs of Preschool Children, J. Nutrition **11**:327, 1936.

2. Daniels, A. L.: Relation of Calcium, Phosphorus and Nitrogen Retention to Growth and Osseous Development: A Long Time Study of Three Preschool Boys, Am. J. Dis. Child. **62**:279 (Aug.) 1941.

Data from Consecutive Magnesium Balance Studies for Three Preschool Boys

Child	Period	Date	Number of Test Days*	Weight, Kg.	Magnesium				Calcium		Calcium
					Ingestion per Kg., Mg.	Excretion in Urine per Kg., Mg.	Excretion in Feces per Kg., Mg.	Retention per Kg., Mg.	Ingestion per Kg., Mg.	Retention per Kg., Mg.	Magnesium Retention Ratio
J. E.	1	9/24	10	18.0	15.4	3.9	10.1	1.4	65	11.3	8.1
		10/15	4	18.2	14.6	3.5	10.0	1.1	64	12.1	11.0
		11/ 5	10	18.6	14.8	4.2	9.7	0.9	65	10.4	11.5
		11/26	10	19.0	14.4	4.2	9.5	0.7	63	8.7	12.4
		12/15	5	19.0	13.9	3.9	9.3	0.7	62	6.9	9.9
		1/14	10	19.2	14.1	3.2	9.6	1.3	62	10.0	7.7
		2/ 4	10	19.3	14.2	3.5	9.6	1.1	63	6.2	5.6
		Average†		18.8	14.5	3.8	9.7	1.0	63	9.3	9.3
	2	3/ 1	5	18.9	12.3	3.1	7.7	1.5	63	12.4	8.3
		3/17	10	19.6	11.6	3.1	7.3	1.2	59	11.9	9.9
		Average†		19.4	11.8	3.1	7.4	1.3	60	12.1	9.3
	3	4/21	10	20.2	11.3	3.5	7.6	0.2	57	10.8	54.0
		5/12	10	20.4	11.0	3.0	8.2	−0.2	57	11.4	....
		6/ 2	10	20.6	10.4	3.3	6.9	0.2	55	13.5	67.5
		6/20	6	20.6	9.8	3.5	6.5	−0.2	54	13.8	....
		Average†		20.4	10.7	3.3	7.4	±0	56	11.9	....
F. V.	1	9/24	10	16.7	15.7	4.5	10.2	1.0	70	10.1	10.1
		10/15	10	17.4	14.8	4.2	9.6	1.0	67	12.8	12.8
		11/ 5	10	18.1	15.1	4.8	9.5	0.8	65	7.4	9.3
		11/26	10	18.7	14.4	3.9	9.8	0.7	63	7.0	10.0
		12/15	5	19.3	12.8	3.8	8.6	0.4	60	10.0	25.0
		1/14	10	18.4	14.1	4.0	9.1	1.0	64	11.2	11.2
		2/ 4	10	18.9	14.1	4.1	9.1	0.9	63	9.2	10.2
		Average†		18.1	14.5	4.2	9.4	0.9	65	9.7	10.8
	2	2/25	10	19.5	11.9	3.2	8.0	0.7	61	4.1	5.9
		3/19	8	19.9	12.0	3.4	7.4	1.2	57	9.3	7.7
		Average†		19.7	11.9	3.3	7.7	0.9	59	6.4	7.1
	3	4/21	10	20.2	10.6	2.7	7.8	0.1	56	12.2	122.0
		5/12	10	20.5	10.5	3.5	7.6	−0.6	56	11.9	....
		6/ 2	10	20.8	10.6	3.2	7.5	−0.1	55	10.9	....
		6/20	6	20.9	9.7	3.7	6.7	−0.7	53	10.3	....
		Average†		20.6	10.4	3.2	7.4	−0.2	55	11.4	....
G. E.	1	9/24	10	14.7	16.3	5.0	10.3	1.0	76	10.9	10.9
		10/15	10	15.1	15.2	4.2	10.2	0.8	72	10.3	12.9
		11/ 5	10	15.5	15.3	4.6	10.0	0.7	73	9.8	14.0
		11/26	10	15.9	15.1	5.2	9.2	0.7	71	7.9	11.3
		12/15	5	16.3	13.9	4.3	8.8	0.8	70	10.6	13.2
		1/14	10	16.2	14.6	3.7	9.6	1.3	70	14.7	11.3
		2/ 4	10	16.6	14.6	4.7	8.5	1.4	70	15.5	11.1
		Average†		15.7	15.1	4.5	9.6	1.0	72	11.4	11.4
	2	2/25	10	17.1	11.4	3.9	7.4	0.1	66	12.2	122.0
		3/18	9	16.9	11.5	3.8	7.8	−0.1	66	8.9	....
		Average†		17.0	11.4	3.8	7.6	±0	66	11.2	....
	3	4/21	10	17.2	11.4	4.0	7.8	−0.3	64	8.3	....
		5/12	10	17.4	12.1	4.6	7.7	−0.2	65	11.4	....
		6/ 2	10	17.4	10.7	4.3	6.3	0.1	64	15.3	153.0
		6/20	6	17.5	11.1	4.5	6.6	−0.1	61	9.8	....
		Average†		17.4	11.4	4.3	7.2	−0.1	64	11.2	....

* This figure does not include the six day preliminary periods.
† Weighted averages.

Each metabolism period consisted of two consecutive five day balance periods preceded by a six day adjustment period to overcome the questionable effects of the less strict diet of the week end at home which occurred once every three weeks.

Magnesium determinations were made with the filtrates incident to the calcium analysis of the foods and excreta as given in the first part of the study, by precipitation as magnesium pyrophosphate, according to Washburn and Shear's [3] modification of the method of McCrudden. Determinations were made in triplicate in all cases. Unless the three determinations checked to within 1.5 per cent or less, a second series of tests was made.

The highest intake of magnesium (period 1, table) averaged 14.5 mg. per kilogram for each of the 2 older boys, J. E. and F. V., and 15.1 mg. per kilogram for the youngest, G. E. If one estimates on the basis of food intake, each boy received 17 mg. per hundred calories. The next lower intake (period 2) averaged 14 mg. per hundred calories, or 11.8, 11.9 and 11.4 mg. per kilogram, respectively, for the 3 boys, while the lowest intake tested (period 3) averaged 13 mg. per hundred calories, or 10.7, 10.4 and 11.4 mg. per kilogram for the 2 older boys and the youngest one, respectively.

Although there was some variation in the magnesium retentions from period to period, the average retentions for all 3 boys at a given ingestion level were in fair agreement, averaging 1.0, 0.9 and 1.0 mg. per kilogram, respectively. Retentions at the next lower ingestion levels (11.8 and 11.9 mg. per kilogram) were slightly less in 1 case than at the higher levels (0.9 mg. per kilogram) and somewhat higher in another (1.3 mg. per kilogram). The youngest boy, G. E., who ingested 11.4 mg. per kilogram during both period 2 and period 3, retained considerably less in both periods, ±0 and —0.1 mg. per kilogram. Retentions with the lowest ingestions tested averaged ±0 in 1 case and —0.2 mg. per kilogram in another.

The percentages of the ingested magnesium excreted through the feces are consistent at all levels of intake, averaging between 63 and 67 per cent at the highest level, with the less refined cereals, between 63 and 68 per cent with refined cereals and high protein and between 63 and 71 per cent with the low protein, refined cereal diet. Average values for the urinary excretion of magnesium during various periods ranged between 3.1 and 4.5 mg. per kilogram of body weight. Considering averages for a given period, the highest excretion, between 3.8 and 4.5 mg. per kilogram, occurred with the highest ingestions for a given child. Low excretion, however, did not in all cases parallel low ingestion; for

3. Washburn, M. L., and Shear, M. J.: Composition of Bone: XIII. Direct Gravimetric Determination of Ca, Mg and PO_4, J. Biol. Chem. **99**:21, 1932.

example, the 2 older boys excreted practically the same amount per kilogram during periods 2 and 3, whereas the youngest child excreted slightly more during period 3 than during period 2 with the same ingestion.

COMMENT

In the previous study of the magnesium needs of children,[1] ingestions ranged between 11.3 and 19 mg. per kilogram. Retentions between ingestions of 15 and 19 mg. averaged 2.06 mg. per kilogram; with ingestions between 14 and 14.9 mg. (average, 14.4 mg.) retentions averaged 1.15 mg. per kilogram, while with the lowest ingestions tested, 11.3 to 11.9 mg. per kilogram, retentions averaged 0.94 mg. per kilogram. Ingestions in the present study are scaled somewhat lower, the highest averaging 15.1 mg. and the lowest 10.4 mg. per kilogram. At the same level of ingestion (average, 14.5 mg. per kilogram) retentions were approximately the same in the two studies. Similar retentions also obtained at somewhat lower ingestions in both studies, 12 mg. per kilogram (average) in the first study and 11.9 and 11.8 mg. in the present one. With only slightly lower ingestions, 11.4 mg. per kilogram, in the present study, retentions were consistently low, sometimes negative, while with ingestion of 10.7 and 10.4 mg. per kilogram, the lowest values tested, nearly negative or frankly negative balances also prevailed.

In the previous report[1] it was suggested that urinary excretion of magnesium of less than 3.4 mg. per kilogram with low magnesium retentions was indicative of too low ingestions. These findings are borne out in the present study with the 2 older boys, and data obtained for them indicate that 11.8 mg. per kilogram is the lower limit of their physiologic need. During periods 2 and 3, urinary excretions averaged 3.1 and 3.3 mg. per kilogram, respectively, for J. E. and 3.3 and 3.2 mg. per kilogram, respectively, for F. V.; although retentions were slightly higher during period 2 than during period 3, there was apparently no considerable excess. G. E., on the other hand, excreted 3.8 and 4.3 mg. per kilogram in the urine during periods 2 and 3, with ingestions of 11.4 mg. per kilogram, somewhat more than the 2 older boys at the lower levels of magnesium ingestion. Retentions, however, were equally low, averaging for period 2, ± 0 mg. and for period 3, -0.1 mg. per kilogram. If our tentative hypothesis that the adequacy of the magnesium ingestion may be judged in part by the amount of magnesium excreted in the urine is correct, then G. E. had become saturated as regards magnesium during period 1 and therefore needed little during periods 2 and 3. For him 11.4 mg. per kilogram was sufficient for the time being. The sudden drop in the magnesium retention at the lower ingestion level, however, would seem to preclude

this interpretation. Possibly the threshold of renal excretion for magnesium differs for different persons, or there may be other explanations for the difference in the relation of urinary magnesium to magnesium ingestion and retention not yet understood. On the basis of retentions, 11.4 mg. per kilogram apparently was insufficient to cover the minimal requirements of the youngest boy tested, while 10.7 and 10.4 mg. per kilogram were below the physiologic needs of the 2 older boys.

The diet of the children as planned in period 1 contained, it was believed, an optimum amount of all the essential constituents. Milk furnished from 30 to 37 per cent of the total calories and, together with the calcium from the other foods of the diet, supplied from 1.11 to 1.19 Gm. per child per day; protein (during periods 1 and 2, 1.5 Gm. per pound [453 Gm.], and during period 3, 1.2 Gm. per pound) was supplied chiefly by milk, eggs and meat. Vegetables furnished 7 per cent and fruits 13 per cent of the total calories. Each child,[1] received daily, in addition to the vitamins of his diet, not less than 13,000 U. S. P. units of vitamin A from cod liver oil and 3,000 U. S. P. units of vitamin D from cod liver oil and viosterol. The antirachitic effect of the vitamin D was enhanced by a ten minute exposure daily to the ultraviolet rays of a sun lamp. Cereal foods, supplying 13± per cent of the total calories, were lower in the diets of the children studied than is often advocated, but since it has been observed that children eat less when taking devitaminized high cereal diets,[4] less cereal was given in order that more fruits and vegetables might be included to make up for the possible vitamin and mineral deficiencies of the cereal foods selected. When cereal foods in the diets given were obtained from whole grain breakfast cereal and commercial whole wheat bread, sufficient magnesium was furnished. The substitution of the more refined cereal foods, together with a slight change in the vegetable moiety to meet the caloric needs incident to growth, decreased the magnesium ingestion to the lower limits of physiologic need (period 2).

In the diets of period 1 and period 2, eggs and meat furnished from 8 to 10 per cent of the magnesium. During period 3, the meat and eggs of the diet were decreased, and thus the protein was lowered from 3.4 Gm. to 2.6 Gm. per kilogram, a value more nearly in accord with the actual needs of the average well nourished child of the age considered. This change reduced the magnesium ingestions from these sources by approximately 50 per cent. In order to compensate for this decrease in the caloric value of the diet, fruit and vegetables, as well as bread, were increased slightly; in spite of this, the magnesium ingestions were lower in 2 cases in period 3, and in all cases were below the needs of the children studied.

4. Daniels, A. L., and Everson, G.: A Study of Anorexia in Preschool Children, J. Home Econ. **27**:43, 1935.

The children at the beginning of the study were considerably retarded in their skeletal development, although they were well within the standards of weight for height. During the period of observation, they were gaining in both height and weight at a considerably faster rate (from 44 to 73 per cent in height and from 44 to 167 per cent in weight) than the average for their respective ages given by the Iowa Child Welfare Research Station.[5] It is possible, therefore, that a child growing less rapidly, that is, one who is more nearly in an optimum physical condition, may need less magnesium. However, the frequency of the negative balances at the lowest levels, 10.4 to 10.7 mg. per kilogram, and the occasional low, often negative, retentions with ingestions averaging 11.4 mg. per kilogram led us to conclude that magnesium ingestions of the preschool child should not fall below 11.8 mg. per kilogram. These values are slightly lower than those of the previous study,[1] in which it was concluded that 13 mg. per kilogram would suffice for the child of the age considered. The nearness of these figures, 13 mg. in the former study, 11.8 mg. in the present study and "something over 10 mg." for slightly older children, as reported by Petrunkina,[6] points to the conclusion that the magnesium requirement for children from 4 to 6 years is between 11.8 and 13 mg. per kilogram. These ingestions are comparable to those in the studies of Souders, Hunscher, Hummel and Macy [7] and Hummel, Hunscher and Macy.[8] It should be noted that the lower figure, 11.8 mg., is based on results obtained with children who previously had received sufficient magnesium, as indicated by their high retentions over a considerable period. Possibly children less well stocked will need more for a time, at least. The consistently high retentions at the beginning of the study and following the Christmas vacation, as well as the many high retentions in the previous study, suggest that the diets of children may be low in this particular element. Thus, for the "average child," the 13 mg. per kilogram as given in the former report may be more nearly safe, since it allows for growth and for the factor of safety which always must be taken into consideration in planning diets for children.

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5. Physical Traits of Young Children, Iowa Child Welfare Research Station, State University of Iowa, Am. J. Dis. Child. **38**:541 (Sept.) 1929; Physical Traits of Iowa Infants, Iowa Child Welfare Research Station, State University of Iowa, ibid. **42**:1137 (Nov.) 1931.

6. Petrunkina, A.: Ueber die Bilanzen von Stickstoff, Kalk, Magnesium, Phosphor und Eisen bei Kindern von 7-8 Jahren, Ztschr. f. Kinderh. **56**:219, 1934.

7. Souders, H. J.; Hunscher, H. A.; Hummel, F. C., and Macy, I. G.: Influence of Fluid and of Evaporated Milk on Mineral and Nitrogen Metabolism of Growing Children, Am. J. Dis. Child. **58**:529 (Sept.) 1939.

8. Hummel, F. C.; Hunscher, H. A., and Macy, I. G.: Effect of Irradiated Milks on Storage of Nitrogen and Acid-Base Minerals in Children, Am. J. Dis. Child. **58**:753 (Oct.) 1939.

Study of the magnesium content of the foods indicates that diets furnishing this amount may be more readily obtained by using whole grain cereals than more highly refined cereals, especially if it is desired to keep the cereal foods low in a particular diet, as is often the case in diets of children in which milk and eggs supply the larger proportion of the protein.

With the exception of period 3, when magnesium ingestions apparently were near or below the physiologic minimum, it is believed that in each period enough of all metabolites, particularly calcium and magnesium, was supplied to make evident any naturally occurring relation; therefore, successive determinations of the magnesium and calcium balances of the 3 boys during the period of rapid growth offered an opportunity to test the metabolic interrelation of these two essential constituents. To this end, average calcium and magnesium retentions per kilogram for each ten day balance period, together with the calcium-magnesium retention ratios, have been listed. In order to reduce to a minimum the influence of experimental errors in analytic determinations of the aliquots tested, which may be greatly exaggerated when multiplied by the totals and therefore may give spurious values for single periods, average ratios for periods 1 and 2 also have been compared.

The calcium-magnesium retention ratios for single metabolism periods show considerable variation, between 5.6 and 67.5 for J. E., between 5.9 and 122 for F. V. and between 10.9 and 153 for G. E. Ratios estimated on averages for entire periods, however, show greater constancy, 9.3 and 10.8 for the two older boys, J. E. and F. V., and 11.4 for the younger one, G. E., during period 1. During period 2 the ratios were 9.3 and 7.1, respectively, for the 2 older boys. Concomitant with the greater gains in height and weight of the 3 boys were the calcium retentions, which were found to be higher than those obtained for well saturated children of these ages (Outhouse and associates [9]); therefore, if there is any optimum ratio of calcium and magnesium, the calcium-magnesium ratios of the boys under consideration, it is believed, should be comparable to those of young tissues. Givins and Macy [10] have reported such ratios for human fetuses. Of the 25 cases reported, the ratios in 14 ranged between 9.3 and 15.7 and were comparable to those of the 3 boys when they were receiving diets containing sufficient magnesium. Medes and Humphrey [11] found the calcium-magnesium ratio for newborn rats to be 6.3. As the animals

9. Outhouse, J.; Kinsman, G.; Sheldon, D.; Twomey, I.; Smith, J., and Mitchell, H. H.: The Calcium Requirements of Five Pre-School Girls, J. Nutrition **17**:199, 1939.

10. Givins, M. H., and Macy, I. G.: The Chemical Composition of the Human Fetus, J. Biol. Chem. **102**:6, 1933.

11. Medes, G., and Humphrey, G. J.: Magnesium Content of Normal Rats at Different Ages, J. Biol. Chem. **74**:149, 1927.

increased in age, the ratio decreased, 30 day old rats averaging 15.2, 90 day old animals 21.1 and adult rats 25.3. The calcium of the body increases faster than the magnesium. Calcium-magnesium ratios, at the various stages of development, however, do not necessarily imply that these metabolites are metabolically interrelated, but merely that they exist in the normally developing organism in these relations. Seemingly an organism may be high in one element and low in another and, for a time at least, may appear to be in a condition of physical well-being. For example, during period 3 F. V. and J. E. were retaining considerable calcium, while their magnesium retentions were low, and sometimes negative. In studies with rats, Medes [12] found that the percentage of magnesium in the body increased slightly with high magnesium diets, while the percentages of calcium and phosphorus were unaffected. With low magnesium diets, the magnesium decreased slightly. The amount in the skeletons of rats fed a deficient diet was found to be less than that in skeletons of control rats (Duckworth and co-workers [13]). The skeleton seemingly functions as a reserve of magnesium on which the soft tissues can draw in time of need; thus a slight deficiency may exist for a considerable period without obvious manifestations. Tufts and Greenberg [14] observed that rats fed a low magnesium diet made fairly good growth up to the time hyperirritability was manifested and that the magnesium of the soft tissues was only slightly reduced. Just how long a condition of subminimal retention in man can continue without some physical manifestation is unknown, as are the characteristics of a less than optimum retention for a considerable period. "Apparently the animals hold on tenaciously to their acquired store of magnesium, but can accumulate little or no extra magnesium . . ." [14] The many high retentions of the children of the previous study and the low retentions with diets which seem to be adequate suggest that a magnesium deficiency may be more frequent than is appreciated. The untoward effects of a low magnesium diet over a considerable period may be related to some of the now baffling diseases of mankind.

SUMMARY

Successive studies of magnesium and calcium balance at three levels of magnesium ingestion have been made with 3 boys of preschool age during a nine month period of observation. Calcium ingestions were as

12. Medes, G.: Magnesium Metabolism on Purified Diets, J. Biol. Chem. **68:** 295, 1926.

13. Duckworth, J.; Godden, W., and Warnock, G. M.: The Effect of Acute Magnesium Deficiency on Bone Formation in Rats, Biochem. J. **34:**97, 1940.

14. Tufts, E. V., and Greenberg, D. M.: The Biochemistry of Magnesium Deficiency: I. Chemical Changes Resulting from Magnesium Deprivation, J. Biol. Chem. **122:**693, 1938.

constant as possible throughout the study, slight changes from period to period being due to differences in the composition of the different food purchases and, when considered on the basis of body weight, to the gains in weight of the children. In order to ascertain if there is any constant interrelation between calcium and magnesium, calcium-magnesium retention ratios were determined for each metabolism period, as well as averages at each level of magnesium ingestion. With magnesium ingestions between 11.8 and 14.5 mg. per kilogram of body weight, average retentions for the 3 boys were almost constant, although there was considerable variation from period to period. With lower ingestions, between 10.4 and 11.4 mg. per kilogram, retentions varied between being just positive and frankly negative. It is concluded from these results that 11.8 mg. per kilogram is the minimal amount that should be included in the diet of the child of preschool age. Judged by retention and urinary excretions of magnesium, ingestions at this level provide no considerable margin of safety. The average calcium-magnesium retention ratios during periods of positive calcium and magnesium retention were fairly constant; retentions during individual balance periods, however, varied widely, and although the retention ratio of the averages corresponded to the calcium-magnesium ratios of rapidly growing tissues (human fetuses), there was not sufficient evidence to conclude that these two substances are metabolically dependent on each other.

Case Reports

ERYTHROBLASTIC LEUKEMIA

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The presence of nucleated red cells is usual in cases of chronic leukemia, especially of chronic myelogenous leukemia. It is well known that in some cases of myelogenous leukemia large numbers of nucleated red corpuscles are present, particularly subsequent to treatment (Forkner [1]). Von Leube [2] in 1900 described a rapidly progressive disorder of the blood characterized by changes which suggested both pernicious anemia and myelogenous leukemia. The term leukanemia which he used was not widely accepted. It is probable that in the cases in which the diagnosis of leukanemia was made both pernicious anemia and chronic myelogenous leukemia were present, for such cases were reported later by many authors, for instance, by Beiglböck,[3] in 1934. Rich and Schiff [4] in 1936 reported a case of pernicious anemia with chronic lymphatic leukemia. Italian authors used the term erythroleukemia for cases of polycythemia with leukemia or with the leukemic blood picture. According to di Guglielmo,[5] such a blood picture indicates severe impairment of the erythropoietic function of the bone marrow of either the normoblastic or the megaloblastic type; the cases in which the derangement was of the latter type include those reported under the name leukanemia. Penati [6] in 1937 reported a case of what he called "leucemia megaloblastica acuta." In this case the percentage of megaloblasts in the peripheral blood was from 16 to 24.

From the Department of Pediatrics of the University of the Philippines College of Medicine, Dr. José Albert, Head.

1. Forkner, C. E.: Leukemia and Allied Disorders, New York, The Macmillan Company, 1938.

2. von Leube, W.: Berl. klin. Wchnschr. **37**:851, 1900.

3. Beiglböck, W.: Wien. klin. wchnschr. **47**:962, 1934.

4. Rich, M. L., and Schiff, L.: Ann. Int. Med. **10**:252, 1936.

5. di Guglielmo, G.: Folia med. **3**:319, 1917; **6**:1, 36, 55, 81 and 101, 1920; Rassegna clin. sc. **10**:13, 1932.

6. Penati, F.: Minerva med. **2**:401, 1937.

Malmberg,[7] Opitz,[8] Solmitz [9] and many others observed that in cases of chronic myelogenous leukemia in children many erythroblasts were present in the peripheral blood.

We have seen a man who had 18,400 white cells per cubic millimeter of peripheral blood, with myeloblasts and myelocytes and 47 nucleated red cells for each 100 leukocytes. The myelogram was as follows:

Basophils	2.0
Basophilic myelocytes	2.0
Juvenile forms	0.4
Eosinophils	
Stab forms	...
Segmented forms	0.4
Myeloblasts	10.0
Promyelocytes	4.0
Myelocytes	6.8
Neutrophils	
Juvenile forms	12.4
Stab forms	10.4
Segmented forms	47.2
Lymphocytes	3.6
Monocytes	0.8

There were 547 nucleated red cells per 250 white cells (218.8 for each 100). Of these, 283 were normoblasts, 90 were basophilic erythroblasts, 69 were macroblasts, 98 were proerythroblasts and 7 were mitotic red cells. This patient, however, had been treated with roentgen rays, and the presence of the large number of immature nucleated red cells in the blood was probably due to stimulation of the bone marrow by the treatment. Such patients are frequently observed.

The case we are reporting is quite different. The patient in this case, who was in the last stage of leukemia, for which she had received no treatment, showed a marked increase in the number of erythroblasts in the peripheral blood and in the bone marrow, which has not previously been described so far as we know.

REPORT OF A CASE

V. T., a girl aged 2 years 3 months, was admitted to the Philippine General Hospital on Sept. 2, 1940 with the chief complaints of a hard mass in the left side of the abdomen and bleeding from the gums.

History.—The present illness was of four months' duration and had begun with the oozing of blood from the gums. The oozing became more profuse when the lips exerted pressure on the gums. The hard mass in the left side of the abdomen was noticed about two months later; at first it was small and about at the level of the umbilicus. The mother noticed that the mass seemed

7. Malmberg, N.: Acta pædiat. **4**:410, 1925.
8. Opitz, H.: Monatschr. f. Kinderh. **48**:193, 1930.
9. Solmitz, W.: Ztschr. f. Kinderh. **38**:146, 1924.

to enlarge rapidly and that it later extended from the costal arch to the level of the iliac crest on the left and that the abdomen bulged. The child became progressively paler, thinner and weaker. Since two months after onset she had had intermittent fever. She became dyspneic and had a cough which was productive of mucoid material. One month before admission she became drowsy and preferred to stay in bed. The bleeding from the gums was intermittent; there was slight bleeding on admission.

There was nothing of importance in the previous history except that she had had a cutaneous disorder, probably scabies, at the age of 1 year, and there were scars from scratch marks on the extremities. The father had asthmatic attacks, the mother was healthy and 9 siblings were living and well.

Physical Examination.—The child was febrile, dyspneic, and apathetic; there were bleeding from the gums and a foul breath. She weighed only 7.2 Kg. She was rather poorly developed, emaciated and pale. The conjunctivas were pale, and the gums and teeth were stained with clotted blood. The tonsils, especially the one on the right, were much enlarged, with a necrotic surface covered with a grayish, foul-smelling material, but not with a distinct membrane, and both showed signs of gangrenous tonsillitis. The cervical glands, especially on the left, were enlarged. The heart beat rapidly and except for booming sounds appeared normal. Examination of the lungs disclosed crepitant and subcrepitant rales posteriorly and anteriorly. The abdomen was bulging, and its superficial veins were prominent. The abdominal wall was tense, but there was no tenderness on palpation. The liver was palpable 4 fingerbreadths below the costal arch. The greatly enlarged, rather hard spleen had sharp edges and extended from the iliac crest to the anterior iliac spine.

Laboratory Data.—Examination of the peripheral blood showed a hemoglobin content (Sicca) of 17 per cent (3 Gm. per hundred cubic centimeters), 1,530,000 red cells and 72,000 white cells, of which 3.2 per cent were eosinophils, 15.6 per cent myeloblasts, 10 per cent promyelocytes, 11.6 per cent myelocytes, 17.2 per cent juvenile forms, 12.4 per cent stab forms, 29.6 per cent segmented neutrophils, 0.4 per cent lymphocytes and 2 per cent monocytes. There were 1,359 nucleated red cells per 250 white cells (533.6 for 100). Of these, 1,245 were normoblasts, 60 were basophilic erythroblasts, 38 were macroblasts, 9 were proerythroblasts, 4 were megaloblasts and 9 were mitotic red cells. Examination of a specimen of bone marrow obtained by sternal puncture showed 312,000 cells per cubic millimeter.

The myelogram was as follows:

Basophils	...
Basophilic myelocytes	...
Juvenile forms	0.5
Eosinophils	
Stab forms	—
Segmented forms	1.0
Myeloblasts	7.0
Promyelocytes	6.5
Myelocytes	15.0
Juvenile forms	26.5
Stab forms	12.5
Segmented neutrophils	31.0
Lymphocytes	—
Monocytes	1.0

There were 2,029 nucleated red cells per 200 white cells (1,014.5 per hundred). Of these, 1,767 were normoblasts, 160 were basophilic erythroblasts, 55 were macroblasts, 27 were proerythroblasts, 7 were megaloblasts and 13 were mitotic red cells. There were Jolly bodies, Cabot ring bodies, metachromatic erythrocytes and basophilic stippled cells but no megakaryocytes.

Course.—The patient remained so dyspneic and drowsy that further examination was impossible, and she died thirty-one hours after admission.

Autopsy.—(Dr. de la Cruz, of the department of pathology.) The body was that of a fairly well developed, poorly nourished Filipino girl, 2 years of age; it was 75 cm. long and weighed 6.9 Kg. The wound from a recent sternal puncture was present.

Abdomen: The abdomen bulged slightly. The liver and the spleen could be palpated several fingerbreadths below the costal arch. There was a small amount of subcutaneous fat, and the musculature was poorly developed. The abdominal lymph nodes were enlarged and pale.

Heart: There were a few "chicken fat" clots in the right side of the heart. The cardiac valves were normal.

Lungs: The right lung weighed 150 Gm. and the left 103 Gm. There were patches of bronchopneumonia on both lungs, especially on the dependent portion of the right lung. On section the patches were firm and grayish red and exuded a small amount of sanguinopurulent fluid on pressure. The peribronchial and mediastinal lymph nodes were enlarged but not caseous.

Spleen: This organ weighed 245 Gm. Its color was reddish; the borders were much rounded, and the capsule was smooth but tense. On section the splenic nodules were prominent.

Liver: The liver weighed 675 Gm. It was yellow, with rounded borders and a smooth capsule. On section the outer surface had a fatty appearance, the organ was somewhat soft and bulged at the edges.

Gallbladder and biliary passages: These structures appeared normal.

Pancreas: This organ weighed 26 Gm. and was pale and firm.

Intestines: The small intestine was 390 cm. and the large intestine 70 cm. in length. The mucosa appeared moderately congested. The lymph follicles of the ileum were moderately prominent. There were no ulcerations and no intestinal parasites.

Adrenals: These glands weighed 6 Gm. each and were apparently normal.

Kidneys: The combined weight was 18 Gm. The capsules were not adherent. The cortices were yellowish, with pinhead hemorrhages. The outer surfaces and the pelves appeared normal.

Tonsils: These glands were necrotic and grayish, with rugged edges and bases.

Bone Marrow: Marrow from the right femur was hyperplastic.

Bacteriologic Data: Cultures of material from the tonsils showed many gram-positive cocci, some gram-negative bacilli and many streptococci and staphylococci. A culture of blood from the heart was sterile after forty-eight hours.

Histologic Examination.—There was cellular infiltration in the portal area and extending throughout the lobe of the liver, and the sinuses were dilated. The liver cells showed atrophy and fatty degeneration. The cellular elements consisted of small and large mononuclear cells. The small cells resembled lymphocytes, with a pink cytoplasm (erythroblasts). The large cells had relatively large, deep-

staining nuclei and a small amount of smooth, bluish-staining cytoplasm. Mixed with these cells were polymorphonuclear leukocytes.

Leukemic infiltrations of the same character were found in various other structures, such as the spleen, the lymph nodes, the intestinal submucosa, the lungs and the heart.

COMMENT

Clinically the disease in this case was doubtless leukemia, but whether it was acute or chronic could not be determined. The stomatitis was rather in favor of the diagnosis of acute leukemia, while the excessive enlargement of the liver, the spleen and the lymph nodes was a symptom more characteristic of chronic leukemia. The hemogram and myelogram, as well as the histologic data, however, were characteristic of chronic myelogenous leukemia. The marked erythroblastosis was unusual; it is observed in this degree only in cases of hydrops foetalis congenitus or icterus gravis familiaris neonatorum. In our case there were five times as many nucleated red cells as white cells in the peripheral blood and ten times as many in the bone marrow. In the histologic sections myeloid metaplasia was evident, and many nucleated red cells were observed. Even in the lumen of the blood vessels a striking number of nucleated red cells were present. The erythroblastosis, however, was characterized by a predominance of normoblasts, not megaloblasts. The high white cell counts in the peripheral blood and the bone marrow were not really counts of white cells. In the peripheral blood there were around 61,000 nucleated red cells per cubic millimeter of blood and only a few more than 11,000 white cells. In the bone marrow there were more than 280,000 nucleated red cells and only 30,000 white cells. Ninety per cent of the nucleated red cells in the peripheral blood and more than 85 per cent of those in the bone marrow, however, were normoblasts (orthochromatic and polychromatic). We had to deal, therefore, with a normoblastic erythroblastosis in our case, in contrast to the condition in cases of hydrops foetalis congenitus, in which the predominance of immature erythroblasts is characteristic. The total number of white cells was extremely low in our case. In the bone marrow there was evidence of real erythroblastic hyperplasia in the sense of di Guglielmo [5]—anemia with erythropoietic hyperactivity. The organs, however, exhibited real myeloid metaplasia, though nucleated red cells were present everywhere in large numbers.

We have already mentioned hydrops foetalis congenitus. In this disease, according to von Gierke,[10] there are three different histologic pictures: (1) erythroblastosis, (2) leukoblastosis and (3) erythroleukoblastosis. It may be difficult in the case of a newborn child to decide whether one is dealing with a case of myelogenous leukemia or of hydrops foetalis congenitus. We should like to stress the resemblance

10. von Gierke, E.: Virchows Arch. f. path. Anat. **275**:330, 1930.

between the histologic data in our case of erythroblastic leukemia and those in cases of erythroleukoblastic hydrops foetalis congenitus. There is no doubt that the same etiologic factor can stimulate both the erythropoietic and the granulocytopoietic functions of the bone marrow at the same time. If there is at the same time an increase in the destruction of the red cells (hemolysis), anemia will develop; if not, polycythemia may be observed.

The blood picture in our case was that of chronic myelogenous leukemia. Acute myelogenous leukemia must be ruled out because of the presence of granulocytes in all stages of maturation. There were in the peripheral blood, as well as in the bone marrow, myeloblasts, promyelocytes, myelocytes and juvenile, stab and segmented cells but there was no hiatus leukemicus, the main symptom of acute leukemia. The histologic sections gave further evidence for the diagnosis of chronic myelogenous leukemia, for in them, too, there were myeloblasts, myelocytes and more mature neutrophils in the leukemic infiltrations. The marked enlargement of the spleen, the liver and the lymph nodes again was more in favor of the diagnosis of chronic myelogenous leukemia. Buccopharyngeal necrosis is observed in cases of acute leukemia; it results from necrosis of a leukemic infiltration. But this necrosis can occur in the last stage of chronic leukemia.

Anemia as severe as that in our case (hemoglobin content of 17 per cent, that is, about 3 Gm. of hemoglobin per hundred cubic centimeters, and less than 1,000,000 red cells per cubic millimeter) is most likely to occur in cases of chronic leukemia of longer duration, though it is not exceptional in cases of acute lymphatic leukemia. However, acute myelogenous leukemia runs so stormy a course in early infancy and childhood that there is usually not time enough for the development of severe secondary anemia.

The patient died after only thirty-one hours in the ward; so we did not have time to complete our investigation on the reticulocyte and platelet counts. But with such exaggerated erythroblastosis there is no doubt that the reticulocyte count must have been high. With regard to the platelet count, we only stress that we did not find any megakaryocytes in the bone marrow smears; so it can be supposed that in our case there was secondary thrombopenic purpura, which is normal in acute and not extraordinary in chronic leukemia. It is claimed that in many cases of chronic myelogenous leukemia the megakaryocyte count in the bone marrow is high and that megakaryocytes appear even in the peripheral blood. On the other hand, it is claimed that the cells considered as megakaryocytes in these cases are not really megakaryocytes but only giant neutrophils. In our cases of chronic myelogenous leukemia there has been no megakaryocytosis but there has been marked megakaryocytopenia. We know that in cases of chronic myelogenous leukemia the

thrombocyte count can be high in the earlier stages of the disease but never in the last stage, that is, a few hours or days before death.

If our case is an example of chronic myelogenous leukemia, it is probable that the disease was either congenital or acquired in early infancy. There are many cases in the literature considered as examples of congenital leukemia, for instance that of Malmberg [7] (first symptoms at the age of 5 months) and that of Solmitz [9] (first signs at the age of 3 months), in which the patients died of chronic myelogenous leukemia in the second year of life.

SUMMARY AND CONCLUSIONS

The case of a 2¼ year old girl with chronic myelogenous leukemia is presented. The patient died thirty-one hours after admission to the hospital. The observations on the blood and the bone marrow as well as the histologic sections were characteristic of chronic myelogenous leukemia. The most striking feature in the case was the marked erythroblastosis. There were 61,000 nucleated red cells per cubic millimeter in the peripheral blood and more than 280,000 in the bone marrow. The majority of the nucleated red cells were normoblasts. The clinical diagnosis was chronic myelogenous leukemia and the hematologic diagnosis was severe erythroblastic anemia with chronic myelogenous leukemia; so the final diagnosis in the case was erythroblastic leukemia. The similarity between the data in this case and those in cases of the so-called erythroleukoblastic type of hydrops foetalis congenitus is discussed. The unknown cause of chronic myelogenous leukemia may stimulate not only the granulocytopoietic tissue but, exceptionally, the erythropoietic tissue of the bone marrow.

CONGENITAL ABSENCE OF THE RIGHT LUNG

ITS OCCURRENCE IN A HEALTHY CHILD

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Congenital absence of a lung is a rare occurrence. In surveying the literature, we found only 40 genuine cases on record. Although most of the patients have been infants, the condition has been demonstrated in several adults of advanced age. No sex predilection is evident in the reported cases. The left lung has been the aplastic one slightly more often than the right. One instance of agenesis of both lungs in a fetus of 8 months [1] has been described.

Schneider,[2] in his anatomic classification of pulmonary agenesis, described three main types of the abnormality. In the first type, which he called true aplasia, there is no trace of lung, bronchus or vascular supply on the affected side. In the second type the bronchus is represented by a small outpocketing from the trachea which is supported by a ring of cartilage; no lung tissue is present. In the third type, which he referred to as extreme hypoplasia rather than aplasia, the bronchus is fully formed but is reduced in size and ends in a fleshy structure without lobes which lies within the mediastinum. More than half of the cases in the literature are of the first type. Only 5 cases [3] of the third type have been recorded.

According to the present day conception [4] of the developmental anatomy of the bronchopulmonary system, the two bronchial buds arise in the embryo by evagination from the primordial trachea before the end of the fifth week. These primitive lung buds, by progressive branch-

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1. Schmit, H.: Ein Fall von vollständiger Agenesie beider Lungen, Virchows Arch. f. path. Anat. **134**:25-32, 1893.

2. Schneider, P., in Schwalbe, E.: Die Morphologie der Missbildungen des Menschen und der Tiere, Jena, Gustav Fischer, 1913, vol. 3, pt. 2, pp. 817-321.

3. Hurwitz, S., and Stephens, H. B.: Agenesis of the Lung: A Review of the Literature and Report of a Case, Am. J. M. Sc. **193**:81-87 (Jan.) 1937. Choisser, R. M., and Bloedorn, W. A.: Agenesis of the Lung, Internat. Clin. **2**:243-252 (June) 1939.

4. Arey, L. B.: Developmental Anatomy, ed. 3, Philadelphia, W. B. Saunders Company, 1937, p. 210.

ing, eventually give rise to the bronchial tree, from the terminal tubules of which arise small outgrowths which constitute the alveoli. When there is complete absence of a main stem bronchus, therefore, the anomaly must have had its origin very early in embryonic life. In cases in which the main stem bronchus is either rudimentary or more or less fully formed, the failure of development presumably occurred in a correspondingly later period.

In all but 1 [5] of the reported cases the external symmetry of the thorax was maintained despite the pulmonary agenesis. Filling of the potential space by the displaced mediastinal contents and a portion of the hypertrophied contralateral lung at an early stage of development apparently prevents contraction of the affected hemithorax. In a number of cases a collection of fluid was present on the involved side. Various other congenital anomalies have been noted in cases of aplasia of a lung. Absence of the ipsilateral pulmonary vessels is a virtually constant feature. Manifold defects in other parts of the cardiovascular system are common accompaniments. The trachea is often narrowed and is apt to contain supernumerary cartilaginous rings. Occasionally it divides into several bronchi, all of which enter the single lung. Stenosis of the esophagus, atresia of the anus, absence of the diaphragm, hypoplasia of the face, dermoid of the eye, absence of the pleura, abnormalities in the lobar division of the remaining lung and agenesis of the spleen and the left kidney and ureter have been observed.

We recently encountered an otherwise healthy child who presented unmistakable evidence of congenital absence of the right lung. In 1885, on the basis of a physical examination, Münchmeyer [6] made a diagnosis of unilateral pulmonary agenesis, subsequently verified by postmortem examination, shortly before death in the case of a 2 year old boy with pneumonia. Otherwise, to our knowledge, the diagnosis has never been made clinically in an authentic case.

REPORT OF A CASE

The patient, a girl 3½ years of age, was admitted to Temple University Hospital on Feb. 10, 1941 for diagnostic study. Her family history was irrelevant. Her developmental history was normal. Except for several transient episodes of illness, characterized by a profuse nasal discharge, a mild cough and, at times, noisy breathing, she always had been in excellent health. In the latter part of January 1941, during one of these episodes of illness, roentgenograms of the chest

5. Dyson, I. E.: Congenital Absence of Lung, J. Iowa M. Soc. **24**:442-445 (Aug.) 1934.

6. Münchmeyer, cited by Welsch, K.: Ein Fall von Mangel der rechten Lunge, Frankfurt. Ztschr. f. Path. **36**:192-206, 1928.

were made for the first time, and their appearance prompted the attending physician to advise that the child be hospitalized for further study. At the time of her admission to the hospital the patient was free of symptoms.

Physical examination on admission revealed a well nourished and well developed child who did not appear ill. The abnormal physical features were confined to the thorax. The musculoskeletal framework was normal, and the respiratory excursions were symmetric. The trachea deviated markedly to the right. The percussion note was hyperresonant throughout the left side of the chest; on the right side it was dull anteriorly and almost flat posteriorly. The breath sounds on the left side were loud and vesicular; on the right side they were diminished in volume, being extremely distant posteriorly. No rales were audible. The apical cardiac impulse was diffuse, being of equal intensity from the right nipple to the right anterior axillary line. The heart sounds were heard on the right side,

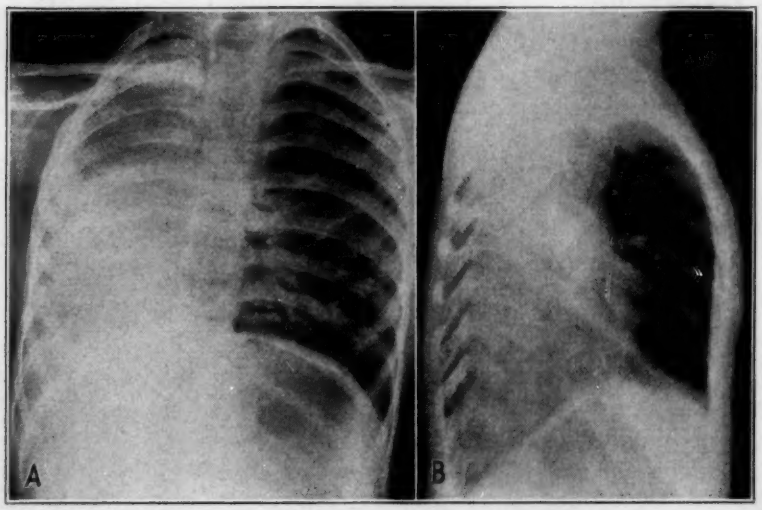

Fig. 1.—Roentgenograms, showing, *A*, that the mediastinal contents are markedly displaced to the right, the right dome of the diaphragm is obscured and no hilar markings are visible on the right side and, *B*, lateral view, that the trachea and heart are displaced posteriorly.

both in front and in back. They were of good quality, and their rhythm was regular. The ventricular rate was 100 per minute. No adventitious sounds were present. The child exhibited no evidence of dyspnea, orthopnea or cyanosis.

The patient's temperature on admission was 98.6 F. Her urine was normal. A blood count showed 5,350,000 red cells, a hemoglobin content of 92 per cent and 7,700 white cells, with 74 per cent mature polymorphonuclear leukocytes. Cutaneous tests for sensitivity to tuberculin gave negative results.

The roentgenographic observations on the chest were identical with those made prior to the child's admission. The ventral projection (fig. 1 *A*) showed a dense shadow in the lower half of the right pulmonic field. The right dome of the

diaphragm was obscured. The heart and the other mediastinal structures were displaced so far to the right that the left cardiac border could not be made out. No hilar markings were visible on the right side. In the lateral projection (fig. 1 *B*) the cardiac shadow was situated posteriorly, aerated pulmonary tissue being interposed between it and the anterior wall of the chest. The lower end of the trachea also was displaced posteriorly. A small quantity of barium mixture administered by mouth was observed fluoroscopically to outline a normal esophagus, which was displaced to the right side. The barium entered the stomach without delay.

Direct inspection of the tracheobronchial tree with a 3.5 mm. bronchoscope was performed on February 13. The mucous membrane was smooth and of normal color. Very little secretion was present. The trachea deviated sharply to the right Its lower end was symmetrically narrowed and was continuous with the left main stem bronchus. A right main stem bronchial orifice could not be found. A second bronchoscopic examination was made on February 25 and a third on March 4. There was no change in the endoscopic appearance.

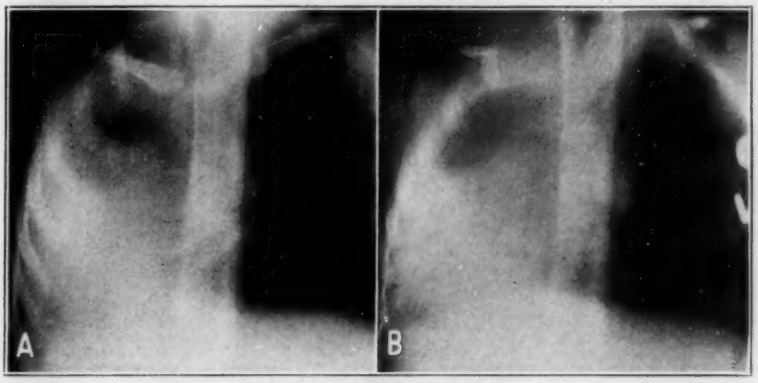

Fig. 2.—Planigrams, showing (*A*) extension of the vascular markings from the left hilus across the midline into the right side of the chest and (*B*) continuity of the air shadow in the right and left sides of the chest.

A planigraphic study of the patient's chest on February 27 added further to the data suggesting congenital absence of the right lung. Vascular markings could be seen extending from the left hilus across the midline into the right side of the chest (fig. 2 *A*). Several of the films showed a sharp delineation of the air shadow in the upper part of the right pulmonic field; the margin of this shadow could be traced as a continuous line all the way from the right lateral wall of the chest to the apex of the left lung (fig. 2 *B*). These observations indicated rather conclusively that the aerated pulmonary tissue in the right side of the chest was part of the hypertrophied left lung which had crossed over above and in front of the heart to fill the space created by the failure of the right lung to develop.

Iodized oil for bronchographic examination was instilled through an intratracheal catheter, under multiplane fluoroscopic guidance, on March 10. During the introduction of the oil the child was in the right lateral decubitus position and was

observed with the horizontal ray of the fluoroscope. In this position the right lateral wall of the trachea was dependent and was filled with puddled oil. There was no escape of the oil into any tract or blind pocket which might represent a stenotic or atretic right main stem bronchus. As is illustrated in figure 3, the trachea and the left bronchial tree were well outlined by the oil. Deviation of the trachea posteriorly and to the right, together with a pronounced narrowing of its terminal portion, was again evident. The oil flowed readily into the bronchi of the upper and lower lobes of the left lung, several branches of which could be followed as they crossed the midline into the opposite side.

The child remained free of symptoms. Except for a slight elevation of temperature which followed each of the bronchoscopic examinations and the administration of the iodized oil, she was afebrile throughout her stay in the hospital. On

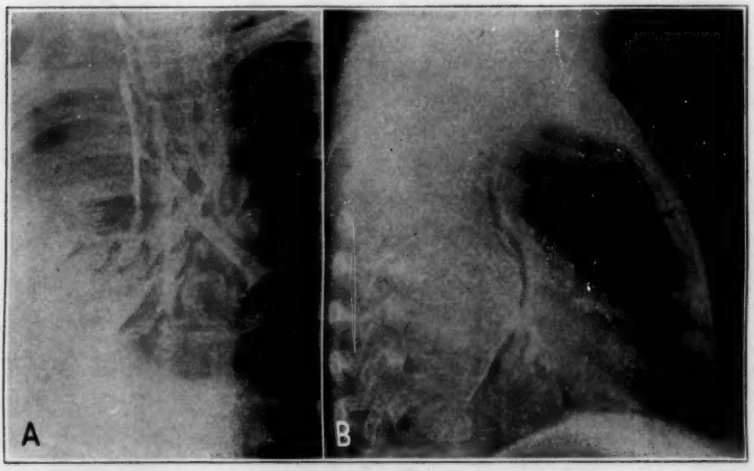

Fig. 3.—Bronchograms, demonstrating, *A*, the narrowing of the lower end of the trachea and the crossing over of the left bronchi to the right side and *B*, lateral view, the outlined trachea and left bronchial tree.

March 15 she was discharged to the care of her private physician. The final diagnosis was congenital absence of the right bronchial tree and right lung.

COMMENT

The case described belongs to the type designated by Schneider [2] as true aplasia. At present there is no evidence that this child has any congenital anomaly other than the absence of her right main stem bronchus and lung and the narrowing of the lower end of her trachea. The roentgenographic observations strongly suggest that no pulmonary vessels are present on the right side, but definite proof of the existence of such a vascular defect must await demonstration at autopsy.

The prognosis for this patient appears to be good. Lack of the respiratory reserve afforded by a normally functioning contralateral lung may prove an insurmountable handicap in the event that her left lung becomes extensively diseased, of course. But, barring such an eventuality, there is no reason to believe that the child's future course will be adversely affected by her pulmonary aplasia. Heerup's [7] discovery of a similar congenital defect in a woman of 72 who had died of cerebral hemorrhage indicates that the condition is quite compatible with longevity.

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7. Heerup, L.: A Case of Absence of the Lung, Hospitalstid. **70**:1165-1176 (Dec. 8) 1927.

SUCCESSFUL TREATMENT OF NOMA WITH SOLUTION OF FORMALDEHYDE

REPORT OF SIX ADDITIONAL CASES

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Since my first report [1] on the use of solution of formaldehyde (British Pharmacopeia) in a case of noma, I have sought to test the usefulness of this preparation further by employing it in a series of cases. Since noma is a comparatively rare disease, no opportunity arose until this year. In the short period of seven months I had the unusual experience of treating 6 patients with the disease, all of them native children of Sierra Leone, West Africa. They came from widely separated towns.

REPORT OF CASES

CASE 1.—The patient, a well nourished girl about 1½ years old, had a perforating ulcer 1½ inches (3.8 cm.) in diameter on her left cheek. The ulcer had a necrotic base and a foul stench and had been present for three days. During the first two days a physician had given mouth washes, to no avail.

Treatment.—The ulcer was dried with cotton, and solution of formaldehyde was applied once daily for three days. No tissue was excised and no mouth washes were given. One gram of sulfanilamide in divided doses was given daily for two days and then 0.5 Gm. daily for three days. Two grains (0.13 Gm.) of quinine ethylcarbonate was given daily, and after two days 2½ grains (0.16 Gm.) of potassium chlorate was administered twice daily.

Result.—After the first day the ulcer began to show improvement, and it was completely arrested within forty-eight hours. The lesion showed no extension after the first application of formaldehyde. The dead tissue sloughed after a week, leaving a surprisingly clean base.

CASE 2.—The patient was a 2 year old boy. Half of his nose and his entire upper lip were eaten away by a foul, gangrenous ulcer, of nine days' duration. The lesion extended to the hard palate, and the upper front teeth had fallen out. The ulcerated area was 2 inches (5 cm.) in diameter.

Treatment.—Solution of formaldehyde was applied daily for four days. One gram of sulfanilamide was given daily for three days and then 0.5 Gm. daily for two days. After two days 2½ grains (0.16 Gm.) of potassium chlorate was administered twice daily for two days. Neither excision nor mouth washes were used.

From the Kamakwie Mission Hospital, Kamakwie, Sierra Leone, West Africa.

1. McMillen, S. I.: Successful Treatment of Noma with Formaldehyde, Am. J. Dis. Child. **50**:1495-1496 (Dec.) 1935.

Result.—After the first application of formaldehyde the ulcer ceased spreading. Dead tissue and a necrotic piece of bone from the maxilla separated after ten days, leaving a clean base. At the end of five weeks the defect had been filled in to a remarkable extent.

CASE 3.—The patient was a 1 year old boy. His entire lower lip and a large proportion of both cheeks were eaten away by a foul ulcer, 4 inches (10 cm.) in diameter. The lesion extended into the lower part of the mouth. The lower front teeth were gone, and the mandible was badly infected. The ulcer had been present for fifteen or twenty days, and the child was badly nourished because of the difficulty in feeding him.

Treatment.—Daily applications of solution of formaldehyde were used for five days. One gram of sulfanilamide daily and 2½ grains (0.16 Gm.) of potassium chlorate twice daily were given for two days. Two grains (0.13 Gm.) of quinine ethylcarbonate was administered daily for seven days.

Result.—On the third day when the child was brought for the third application of formaldehyde, the situation looked hopeless. The ulcer had spread farther on the cheek, the stench was foul and the child was weaker and was anemic. At this juncture the administration of sulfanilamide and potassium chlorate was discontinued. Formaldehyde and quinine ethyl carbonate were the only medicaments used. At the end of the next day there was only slight improvement. At the end of five days the disease was arrested. Eight days after admission the large dry coagulum, about ½ inch (1.3 cm.) thick, began to separate from the cheeks, leaving clean healthy tissue beneath. About three weeks later the necrotic piece of mandible came away. The child made an uneventful recovery. Since the ulcer in this case was much larger than in the others, the patient will have a deformity of the face, but this is not an item of great moment in the African bush.

CASE 4.—The patient a boy about 1 year of age, was admitted April 30, 1940. He had a foul ulcer extending over the upper part of the palate, the inner surface of the left cheek and an area around the lower teeth on the left side. A dark area 1½ inches (3.8 cm.) in diameter on the left cheek showed the extent of the gangrene externally. Most of the teeth on the left side had fallen out. The lesion had been present for ten days. The child also had depigmented spots on the face and the body, the sites of vanishing secondary lesions of yaws. A hard cough betrayed the existence of bronchopneumonia.

Treatment and Course.—On April 30 solution of formaldehyde was applied and 2 grains (0.13 Gm.) of quinine ethylcarbonate was administered. On May 1 formaldehyde was applied and ¼ grain (0.015 Gm.) of sodium potassium bismuthyl tartrate intramuscularly, 15 grains (0.97 Gm.) of sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) in divided doses and 2 grains of quinine ethylcarbonate were given. One of the depigmented yaws spots on the upper lip had become gangrenous over night, and for this reason the bismuth preparation was administered to counteract the yaws. The upper lip, which was now necrotic, was cut away to allow easier application of the formaldehyde to the inside of the mouth. This excision was painless as the line of cutting was more than ¼ inch (0.6 cm.) away from the healthy tissue. There was no bleeding because the blood vessels were thrombosed. The sulfapyridine was given to combat the pneumonia. On

May 2 formaldehyde was applied and 10 grains (0.65 Gm.) of sulfapyridine was administered. On May 3 formaldehyde was again applied and 10 grains of sulfapyridine and 1½ grains (0.1 Gm.) of acetarsone were administered. By this time the infection had spread to a secondary lesion of yaws on the left cheek, where over night another large ulcer had formed. A large circular hole was cut in the left cheek to facilitate the application of formaldehyde and to help dry out the mouth. It was evident that the yaws lesions were furnishing a rich soil for the spread of the noma. Hence it was decided to give acetarsone for the yaws and to treat the anemia, which was severe. The bismuth preparation was not given after the first injection because it was feared that salivation might result from its use. The administration of sulfapyridine was discontinued since the cough had improved. On May 4 and 5 formaldehyde was applied and 1½ grains of acetarsone was administered. On May 6 formaldehyde was again used and 2 grains of quinine ethylcarbonate was administered. There was a persistent but slight spread of the ulcer on the lower aspect of the circular hole in the left cheek. The father rightly suggested that this spread might be due to the saliva's keeping this area moist. On May 7 formaldehyde was applied. By May 8 the disease was definitely arrested. Supportive treatment with acetarsone and quinine ethylcarbonate was given. The child had gained strength, and the ulcer was dry and free of stench. By May 14 healing of the ulcer had progressed rapidly. The parents felt that they had to return the 20 miles (32.2 kilometers) to their home and took the child with them.

Case 5.—The patient, a 1 year old girl, was admitted Sept. 5, 1940. She had a huge ulcer of the right cheek, 2¼ inches (5.7 cm.) in diameter, which extended to the right side of the lower lip, the right side of the nose and to within about ½ inch (1.3 cm.) of the inner canthus of the right eye, which was swollen shut.

Treatment.—Solution of formaldehyde was applied daily, and 2 grains (0.13 Gm.) of quinine was given daily. By September 9 the ulcer was completely dry and the disease was arrested except in the region of the inner canthus of the right eye, which was still swollen shut. Formaldehyde was applied only to the small area near the inner canthus. By September 10 the swelling of the eyelids was reduced. By September 12 the gangrene had advanced to the inner canthus of the right eye. This progression was caused by the tears which kept this area wet because the lacrimal duct had been destroyed. The mother was told to keep the child lying on the right side so that the tears would have to escape over the external canthus. Formaldehyde was applied only in small amounts because of the proximity of the conjunctiva. By September 14 the disease was arrested and no stench could be detected. The conjunctiva was chemotic from the action of the formaldehyde applied to the nearby regions. By October 14 much of the defect on the right side of the face had been filled in.

Case 6.—The patient, a 2 year old girl, was admitted on Sept. 9, 1940. There was an ulcer 1½ inches (3.8 cm.) in diameter on the left cheek, and the angle of the mouth on the left side was almost eaten away. The duration of the lesion was six days. From September 10 to 14 formaldehyde was applied and 2 grains (0.13 Gm.) of quinine administered daily. By September 14 the ulcer was dry and the disease arrested everywhere except at the lower part of the ulcer, where the saliva was draining. The mother was urged to keep the child lying on her right side. By September 15 the disease was completely arrested. On

September 17, a large necrotic piece of the mandible which had separated away was lifted out. On October 15 the mother returned with the child to her town. The defect in the cheek was almost healed.

Quinine ethylcarbonate is given to nearly all children here because of the ever present danger of subtertian malaria. I doubt that it could be considered to have any bearing on the treatment of noma.

In cases 1 and 2, although small doses of sulfanilamide were given, it was believed that the formaldehyde was the only agent important in effecting the cure. In case 3 sulfanilamide therapy was instituted at the beginning because the situation looked hopeless and it was thought that the child should be given every possible aid. The drug was given for only two days, and its administration was stopped when the child's condition was at its worst. Then formaldehyde alone was used, and only then did the child show improvement. In case 4 noma was complicated by yaws and bronchopneumonia. In this case sulfapyridine was given for three days. However, the noma did not begin to abate for three days

Photographs of 2 patients with noma taken on October 3. *A* (case 5), patient four weeks after admission, showing the healthy wound and the defect in the face, which was filling in rapidly. *B* (case 6), patient three and a half weeks after admission, showing the defect in the cheek, which has almost closed.

after the administration of sulfapyridine had been discontinued. Neither sulfanilamide nor sulfapyridine was given in cases 5 and 6 or in the case reported in 1935. The patient in case 4, in which noma was complicated by yaws, was the slowest to respond to treatment. Yaws is caused by Spirochaeta pertenuis. Two organisms are constantly found in the smears of material from the lesions of patients with noma, namely, Spirochaeta vincenti and Bacillus fusiformis. Perhaps the difficulty encountered in treating the patient in case 4 was due to the widely disseminated spirochetes of yaws, which were able to function after the spirochetes of noma were destroyed.

COMMENT

There are four diseases in which S. vincenti and B. fusiformis are the predominating organisms, namely, tropical ulcer, noma, Vincent's angina

and hospital phagedena. Workers in the tropics have been using formaldehyde in the treatment of tropical ulcer for a number of years. In fact, the specificity displayed by formaldehyde in the therapy of tropical ulcer was what led me to use it for noma. Hence, physicians might do well to consider using formaldehyde in the treatment of certain cases of Vincent's angina and hospital phagedena.

Mode of Action of Solution of Formaldehyde.—The arrest of the noma was definitely delayed in several of the cases because of the presence of saliva or tears. Hence the dehydrating action of the undiluted solution of formaldehyde appears to be important. The dehydration extends to a considerable depth and reaches the anaerobic organism. However, I was impressed by the fact that the odor of formaldehyde was noticeable twenty-four hours after the solution had been applied. Perhaps the action of this gas, given off over a long period, is of some importance. If this is true, it is important not to excise all of the necrotic tissue because such tissue is spongy and tends to hold much more of the solution of formaldehyde and to give off the gas for a much longer time than healthy tissue.

Principles of Treatment.—The following points should be borne in mind:

1. Excision should be confined to large, neglected ulcers. Even then it should not cause bleeding or pain. No attempt should be made to excise all of the infected tissue because this procedure is harmful. Hanging shreds of tissue and loose teeth may be removed.

2. The lungs can usually be protected against the irritating vapor of formaldehyde. Cotton can be pushed into the back of the mouth when one is applying the solution in the mouth and into each nostril if one is swabbing the nasal area.

3. It is important to dry the ulcer with cotton before applying the solution of formaldehyde.

4. The applicator should have a generous wad of loose cotton on the end and should be well saturated with the undiluted solution of formaldehyde but not dripping. Care should be exercised so that any excess of the solution does not run back into the pharynx.

5. Applications should be made once daily until there is no sign of further extension and the ulcer has become dry and free from stench. About four or five applications are necessary.

SUMMARY

The daily application of solution of formaldehyde (British Pharmacopeia) is highly efficacious even in cases of advanced noma. In 1 case reported in 1935 and in 6 consecutive cases reported in the present

paper such treatment was used without a death. The mortality rate previously had been about 90 per cent.

Excision should not include all of the necrotic tissue, for such spongy tissue absorbs the formaldehyde and releases it during the following twenty-four hours. Such excision requires no anesthetic and causes no pain or bleeding.

Neither sulfanilamide nor sulfapyridine proved useful.

A mouth wash is not necessary; it may even do harm by washing away the formaldehyde.

PRIMARY INOCULATION TUBERCULOSIS OF THE SKIN

ITS OCCURRENCE IN A FOUR YEAR OLD CHILD

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Little has appeared in the pediatric literature on the subject of traumatic inoculation tuberculosis of the skin with metastasis to the regional lymph nodes. Holt and McIntosh [1] stated that the disorder is comparatively rare and that the primary lesion, in particular, is likely to pass unrecognized because tuberculosis is not considered. A better acquaintance with the clinical manifestations of this lesion would probably result in its being identified more frequently by pediatricians and surgeons.

Tscherning [2] in 1888 reported the case of a servant who wounded a finger with a fragment of sputum cup while attending a tuberculous patient. Tuberculous lymphatic involvement followed, and it was necessary to amputate the finger and to remove the affected glands before recovery ensued.

In 1909 Escherich [3] reported the case of a child with inoculation tuberculosis of the cheek. Klebs [4] mentioned in his book the occurrence of extensive tuberculosis of the inguinal nodes in an infant as the result of a slight prick of the thigh with a safety pin. Epstein [5] in 1912 described the cases of 2 children with inoculation tuberculosis of the ear which followed puncture for earrings.

In 1913 Holt [6] reported the case of a 3 month old infant in whom after ritual circumcision primary inoculation tuberculosis of the prepuce

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From the Division of Pediatrics, Howard University College of Medicine, and the Pediatric Service of Freedmen's Hospital.

1. Holt, L. E., Jr., and McIntosh, R.: Holt's Diseases of Infancy and Childhood, ed. 11, New York, D. Appleton-Century Company, Inc., 1940, p. 1314.

2. Tscherning, E. A.: Sur deux cas d'inoculation tuberculeuse chez l'homme, Cong. p. l'étude de la tuberc., Paris, 1888, vol. 1; cited by Stokes.[10]

3. Escherich, T.: Die Infektionswege der Tuberkulose, insbesondere im Säuglingsalter, Wien. klin. Wchnschr. **22**:515, 1909; cited by Stokes.[10]

4. Klebs, A. E.: Tuberculosis, New York, D. Appleton and Company, 1909.

5. Epstein, A., in Max Kassowitz: Zur Feier seines siebzigsten Geburtstages von Schülern, Freunden und Verehren gewidmete Festschrift, Berlin, Julius Springer, 1912, p. 43; cited by Stokes.[10]

6. Holt, E. L.: Tuberculosis Acquired Through Ritual Circumcision, J. A. M. A. **61**:99 (July 12) 1913.

and the penis developed, with a fatal outcome from miliary tuberculosis. He collected 40 similar cases from the literature. In practically all cases the family of the infant was free from tuberculosis, but the person who performed the circumcision and sucked the penis was tuberculous. The local penile tuberculous reaction appeared within a week and inguinal lymphatic involvement within two or three weeks; systematic generalized involvement, when present, rarely occurred before the third or fourth month. Sixteen of the patients died, the usual cause of death being miliary tuberculosis. Incidentally, in many of these cases the disease was regarded as a syphilitic infection at the onset.

Davis [7] in 1921 described a case in which inoculation tuberculosis of the hand followed the bite of a cat. In 1923 Joyce [8] described 2 cases, one of a mother inoculated on the chin and the other of her 8 year old daughter inoculated on the cheek, presumably by the child's tuberculous father. The previous year Nixon and Short [9] reported 4 cases of so-called tuberculous chancre. One case was that of a mother in whom inoculation tuberculosis of the chin with submental adenopathy developed after she was kissed by her son, who was dying with pulmonary tuberculosis. Another case was that of a 6 year old child, in whom after the receipt of a cut over the patella, which did not heal for six months, enlargement of a lymph node in the groin occurred. Both lesions were proved to be tuberculous, and uneventful healing followed excision of the ulcer and the node. The other 2 cases were similar. In each instance a local tuberculous lesion developed after trauma, with subsequent involvement of the regional lymph nodes.

In 1925 Stokes [10] published an excellent review of the literature and reported 10 cases of primary inoculation tuberculosis of the skin with metastasis to the regional lymph nodes. Six of his patients were children, aged 2, 4, 5, 13, 16 and 17 years respectively.

Krantz [11] in 1931 collected reports of 34 cases of primary tuberculosis of the skin, and Carter and Smith [12] in 1935 reported the cases of 7 children between the ages of 6 and 14 years. In each instance there

7. Davis, H.: Case of Tuberculosis of Skin Following a Cat Bite, Proc. Roy. Soc. Med. (Sect. Dermat.) **15**:9, 1921-1922.

8. Joyce, C.: Tuberculosis of the Skin, M. J. Australia **1**:236, 1923.

9. Nixon, J. A., and Short, A. R.: Tuberculous Chancre, Brit. J. Surg. **10**: 44, 1922.

10. Stokes, J. H.: Primary Inoculation Tuberculosis of the Skin with Metastasis to Regional Lymph Nodes, Am. J. M. Sc. **169**:722, 1925.

11. Krantz, W.: Zentralbl. f. Haut- u. Geschlechtskr. **39**:1, 1931; cited by Kereszturi and Siegel.[13]

12. Carter, B. N., and Smith, J.: Tuberculous Lymphadenitis Secondary to Inconspicuous Healed Traumatic Cutaneous Tuberculous Lesions, J. A. M. A. **105**:1839 (Dec. 7) 1935.

was tuberculous lymphadenitis secondary to an inconspicuous healed traumatic cutaneous tuberculous lesion. Kereszturi and Siegel [13] in 1936 reported the cases of 2 children with primary inoculation tuberculosis of the skin and regional tuberculous lymphadenitis; they also collected 11 additional cases which had appeared in the literature since the report by Krantz in 1931.

A case of probable primary inoculation tuberculosis of the skin with regional lymphadenitis is reported.

REPORT OF A CASE

N. B., a 4 year old Negro boy, was admitted to the Freedmen's Hospital April 29, 1940 because of a "sore on the right knee" and a draining sinus in the right groin. Four months prior to admission the child experienced an insignificant fall, whereby he sustained a slight abrasion of the skin over the right knee cap. The wound, although only a superficial laceration, failed to heal properly, with the result that suppuration and superficial ulceration followed.

About two weeks after the accident a "lump" was discovered in the right groin. This inguinal mass increased progressively in size and eventually ruptured, liberating yellowish pus. An indolent draining sinus ensued. These lesions had not incapacitated the boy, and he had not been put to bed prior to hospitalization. His illness had been essentially afebrile.

The child was born at term after a normal labor and weighed 7 pounds (3,175 Gm.) at birth. He was breast fed for the first six months, at the end of which time an evaporated milk formula was substituted for the breast milk. His development was normal. He had always been in good health except for varicella at 1 year and pertussis at 3 years of age.

The child's mother was 31 years old and was apparently in good health. Roentgenograms were negative for pulmonary tuberculosis. The Wassermann reaction of her blood was negative. The father had been accidentally killed two years previously. He was said to have been in good health at the time of his death. The patient was the youngest of 6 children. The 5 elder siblings were all apparently in good health and had negative reactions to tuberculin tests with the first strength purified protein derivative. There was no history of tuberculosis in the family.

Physical Examination.—The boy was fairly well nourished; he weighed 36 pounds (16.3 Kg.). The tonsils were enlarged and hyperemic. The nasal mucous membranes were injected. Caries was detected in one tooth. The anterior cervical lymph nodes were slightly enlarged bilaterally. The eyes, ears and lungs were normal. A soft systolic precordial murmur was present; however, the heart was of normal size. The liver and the spleen were not enlarged. The axillary and epitrochlear lymph nodes were small, firm, discrete and nontender.

Of special note were two draining sinuses just below the right inguinal ligament (fig. 1). The sinuses were about 1 inch (2.5 cm.) in length and occupied the summit of swollen and tumefied tissue which surrounded them. A creamy discharge oozed from the openings. The surrounding skin was hyperpigmented.

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13. Kereszturi, C., and Siegel, M.: Primary Tuberculosis of the Skin, Am. J. Dis. Child. **51**:847 (April) 1936.

The area of inflammation was indolent and only slightly tender to palpation. The inguinal glands on the opposite side were palpable but not especially enlarged. The back and the spine were normal.

The skin over the right patella (fig. 1) showed a hard raised gray superficial warty growth, measuring 3 by 4 cm. This chief lesion was surrounded by similar satellite excrescences. The usual signs of acute inflammation were absent. The affected skin had lost its normal resiliency; however, it was freely movable and was not adherent to underlying deeper structures. The lesion was homogeneous, and no sinuses were present. The popliteal lymph nodes were not palpable.

Course.—Dr. Henry H. Hazen concurred in the clinical impression of tuberculosis verrucosa cutis. At his suggestion the lesions of the knee and the groin were treated with filtered roentgen rays. In addition to general hygienic measures, a diet rich in vitamins, minerals and fats was prescribed, with sodium chloride and carbohydrates restricted to a minimum. After a period of four months the lesion in the groin healed and the child gained 3 pounds (1.3 Kg.). The verrucous lesion at the knee, however, responded less favorably to treatment. When the patient was last seen, on Feb. 13, 1941, the latter lesion was the site of an exacerbation.

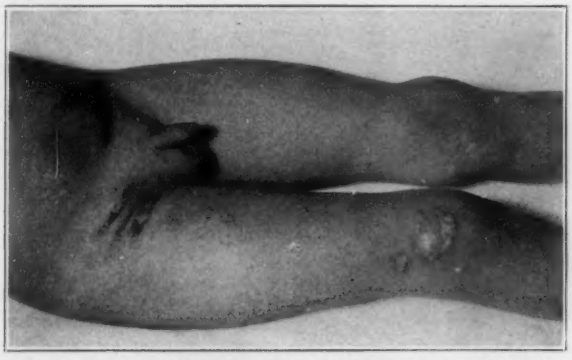

Fig. 1.—The patient, showing partially healed scars from old sinuses in the inguinal region and cluster of gray verrucous lesions at the knee.

Laboratory Data.—The reactions to Hinton and Eagle precipitation tests on the blood were negative. The average of several blood counts showed normal values except for slight relative lymphocytosis. The total leukocyte count was always within normal limits. The urine was normal. Roentgenograms of the skeletal system were normal.

Serial roentgenograms of the chest were reported by Dr. C. H. Kelley and Dr. J. L. Martin, roentgenologists, as negative for evidence of tuberculosis of the lungs or the glands of the hilus. The series of roentgenograms of the chest, taken over a period of six months, was also studied by Dr. T. A. Williston and Dr. Howard Payne, phthisiologists. They expressed the opinion that the roentgenograms were negative for evidence of pulmonary tuberculosis. The latter consultant stated: "A review of the clinical evidence in this case appears to indicate that there has been primary inoculation of the skin with tubercle bacilli in the region of the right knee, with tuberculous metastasis to the inguinal lymph nodes."

The reaction to an intracutaneous test with tuberculin (0.00002 mg. of purified protein derivative) was 4 plus on admission. The result of an intradermal test with tuberculin performed in a child welfare clinic a year previously was reported as negative. The sedimentation rate of the erythrocytes ranged between 15 and 25 mm. per hour.

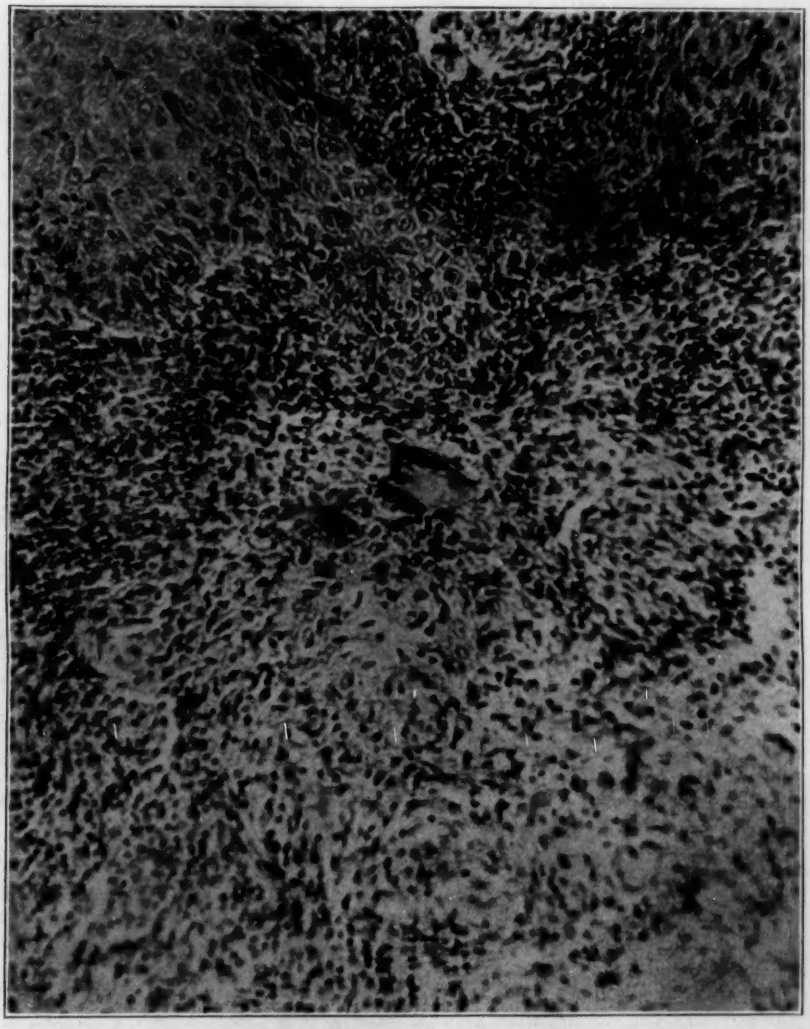

Fig. 2.—Section of skin from knee, showing epidermis and intradermal granulomatous lesion consisting of noncaseating tubercle with surrounding lymphocytic infiltration. Low magnification.

Attempts to recover tubercle bacilli from the lesions late in the course of the disease were unsuccessful. Sporotrichum, Blastomyces and Actinomyces could not be demonstrated in cultures. Tissue was removed from the lesions for pathologic study prior to the institution of therapy.

Biopsy Report on Skin from Right Knee (Dr. R. S. Jason).—A small section of wrinkled skin removed from the region of the right knee showed, on microscopic examination (figs. 2 and 3), several areas of superficial inflammation characterized by the presence of epithelioid and giant cells, lymphocytic infiltration, widening of the interpapillary spaces and hyperplasia of the papillary pegs.

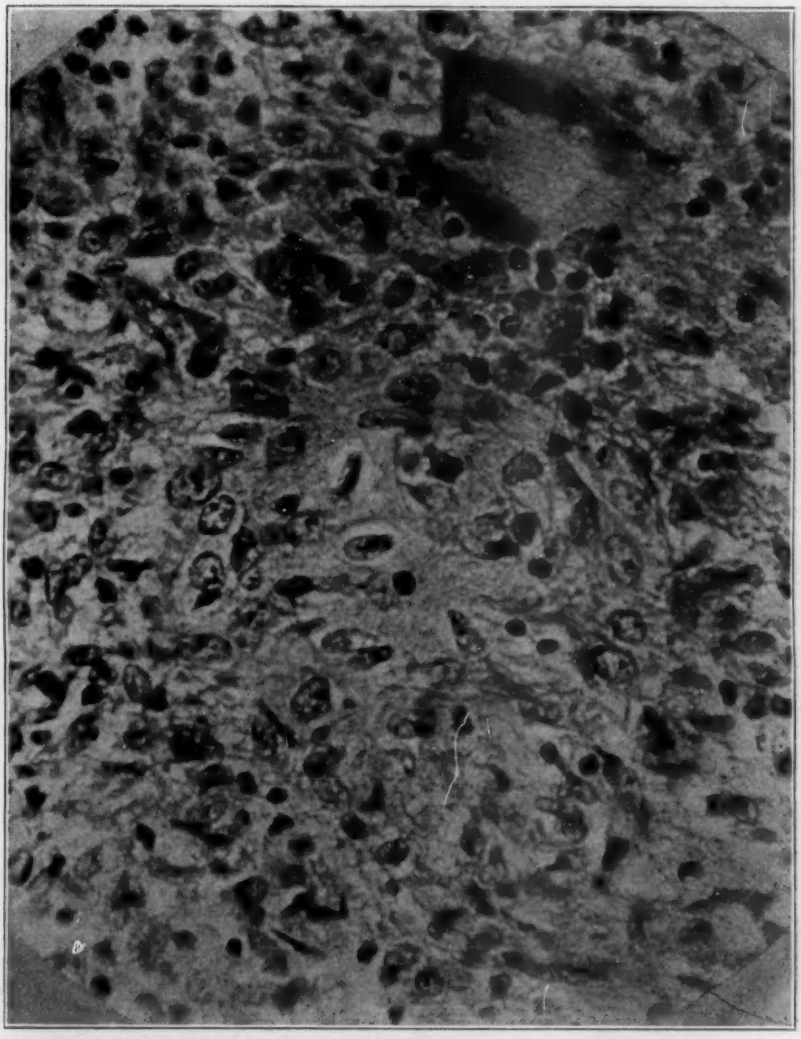

Fig. 3.—Section of skin from knee, showing epithelioid cell tubercle and giant cell but no caseation. High magnification.

Tubercle formation was present, but caseation was absent. The pathologic impression was tuberculosis of the skin.

Biopsy Report on Tissue from Inguinal Lesion (Dr. E. E. Collins).—Examination of a fragment of tissue excised from one of the indolent inguinal sinuses revealed an ulcer on one surface. The base of the ulcer was composed of tuber-

culous granulation tissue in which there were groups of epithelioid cells and numerous Langhans giant cells (fig. 4). The ulcer was in skin covered by markedly acanthotic squamous epithelium. The papillary connective tissue exhibited granulomatous infiltration. Abortive attempts at epithelization of the ulcer surface had resulted in trapping of islands of epithelium deep in the base. Several tubercle-

Fig. 4.—Section of tissue from lesion in groin, showing small segment of epidermis and intradermal granuloma consisting of conglomeration of four small noncaseating tubercles with intervening giant cells and surrounding mantle of heavy lymphocytic infiltration. Low magnification.

like formations composed of whorls of epithelioid cells were observed. Caseation was absent. The microscopic picture was not unlike that of sarcoid of Boeck. The pathologic impression was chronic tuberculous ulcer in the skin of the inguinal region.

COMMENT

Tuberculosis verrucosa cutis [14] usually, if not invariably, is of exogenous origin and is a result of inoculation with bacilli from contaminated objects, the tissues of infected animals or tuberculous sputum. The sites of predilection are the exposed surfaces, particularly the hands and fingers. The lesions begin as small wartlike papules, which increase in number and coalesce to form small verrucous patches, which may be single or multiple. Although the lesions may heal spontaneously, they are usually persistent but comparatively benign.

The origin of the tuberculous lesions in this case in all probability was the exogenous inoculation of the trivial cutaneous wound in the region of the knee with tubercle bacilli. Tuberculosis verrucosa cutis developed at the site of inoculation, and the inguinal lymph nodes became involved by drainage from the infected peripheral area. The tuberculous lesions in the regional inguinal glands became liquefied and formed a cold abscess, which ruptured spontaneously and resulted in sinus formation. The source of the child's direct contact with the tubercle bacilli remains a mystery. In such cases the organisms are often of the bovine type.[15]

The transition from a negative tuberculin reaction a year prior to admission to a positive reaction at the time of hospitalization is at least suggestive of the primary nature of the present lesions. The lack of clinical evidence of tuberculosis elsewhere in the body, the youth of the patient, the insidious development of the lesions and the progressive involvement of the regional lymph nodes furnish additional presumptive evidence of a probable primary tuberculous complex involving the skin and the regional lymph nodes.

Carter and Smith [12] have called attention to the fact that in cases of primary inoculation tuberculosis it is the adenopathy which usually causes the patient to seek medical care. Because of the interval between the onset of the primary cutaneous lesion from inoculation and the appearance of regional adenopathy, the former lesion is often healed or inconspicuous when the physician sees the patient. Hence, the primary focus is frequently overlooked. Stokes [10] cautioned that such an overlooked primary focus may serve for months or years as a "feeder" for a lymphatic lesion and may be responsible for repeated recurrences of adenitis in spite of drainage or excision of the infected nodes. Hence, he suggested that the delayed development of adenopathy after even trifling

14. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, ed. 9, St. Louis, C. V. Mosby Company, 1935, p. 893. MacKee, G. M., and Cipollaro, A. C.: Skin Diseases in Children, New York, Paul B. Hoeber, Inc., 1936, p. 226.

15. Fox, H.: Diseases of the Skin in Infancy and Childhood, in Clinical Pediatrics, New York, D. Appleton and Company, 1930, vol. 16, p. 231.

trauma should lead to examination of the lymphatic drainage area for a possible focus of tuberculosis inoculation.

Stokes pointed out that tuberculosis verrucosa cutis theoretically should be the typical reaction of the previously infected adult to cutaneous inoculation with bacilli. With this type of lesion involvement of adjacent lymphatic strictures and systemic spread are generally not common. On the other hand, inoculation tuberculosis of the skin with extension to the lymph nodes and systemic infection should theoretically be possible only in infancy and early childhood, before systemic infection has resulted in the development of resistance. However, the marked variability in the resistance of the host and the virulence of the micro-organism prevents the too strict application of the foregoing immunologic rule. Apparently one cannot always predict clinically what the character or the course of the lesion in a given patient will be. Such variability of reaction is reflected in the case presented here, in which a local cutaneous verrucous lesion, more commonly observed in the relatively "resistant" adult, was associated with regional lymphadenitis, a lesion typically observed in infants and children. Typical tuberculosis verrucosa cutis is rare in children.[15]

Other conditions, such as lupus vulgaris, syphilis and fungous infections, which might be confused with tuberculosis verrucosa cutis were excluded by clinical, serologic, pathologic and bacteriologic studies.

The histologic picture of epithelioid tubercle formation without caseation and the apparent benignity of the lesions, as well as the absence of demonstrable tubercle bacilli, constitute a clinical syndrome not incompatible with a diagnosis of sarcoidosis of Boeck.[16] However, any effort to exclude sarcoid of Boeck completely would probably be of more academic than practical importance, since this disease syndrome, also, is generally, though not universally, regarded as a peculiar, benign, noncaseating form of tuberculosis.

In view of the rare recovery of acid-fast bacilli from lesions of the "sarcoid" type, the experience of Mellon and Beinhauer [17] is interesting because it supports the allegedly tuberculous nature of this syndrome. These investigators reported the recovery in pure culture of a partially

16. Newns, G. H., and Hardwick, C.: Besnier-Boeck's Disease in an Infant, Arch. Dis. Childhood **14**:78, 1939. Longcope, W. T., and Pierson, J. W.: Boeck's Sarcoid, Bull. Johns Hopkins Hosp. **60**:223, 1937. Harrell, G. T.: Generalized Sarcoidosis of Boeck, Arch. Int. Med. **65**:1003 (May) 1940. Pinner, M.: Non-Caseating Tuberculosis, Am. Rev. Tuberc. **36**:706, 1937; **37**:690, 1938. Benedict, E. B., and Castleman, B.: Sarcoidosis with Bronchial Involvement, New England J. Med. **224**:186, 1941.

17. Mellon, R. R., and Beinhauer, L. G.: The Pathogenesis of Noncaseating Tuberculosis of the Skin and Lymph Glands, Arch. Dermat. & Syph. **36**:515 (Sept.) 1937.

acid-fast organism from the lesions of a patient with noncaseating tuberculosis of the skin and the lymph nodes. Experimentally, this microorganism produced noncaseating epithelioid (sarcoid) lesions in the lungs of guinea pigs. These workers regarded this organism as a "rough" dissociation variant of the bacillus of Koch.

Tuberculosis verrucosa cutis is benign in the sense that the patient's life is seldom jeopardized. However, without treatment the condition may remain active for years. There is no specific therapy. Surgical excision or roentgen therapy is the method of choice for the treatment of local lesions; however, fulguration, application of radium, chemical cauterization, ultraviolet irradiation and heliotherapy are also occasionally used. The general measures include good hygiene, a liberal intake of vitamins and protection from intercurrent infections. Arsenic and the hypophosphites are popular internal remedies. The employment of the so-called Sauerbruch-Hermannsdorfer diet for patients with this type of lesions has many advocates.[13]

SUMMARY

The case of a child with probable primary inoculation tuberculosis of the skin is reported.

The disease is comparatively rare and is likely to pass unrecognized.

The histologic picture was that of noncaseating tuberculosis of the skin and regional lymph nodes.

Unless it is inactivated by local therapy, the primary cutaneous focus may serve for an indefinite period as a "feeder" for the lymphatic lesion.

Dr. Edward L. Howes, of the department of surgery, gave permission to report this case. Dr. Robert S. Jason gave advice in the preparation of the pathologic report. Dr. H. A. Poindexter was responsible for the cultures. The biopsies were made by Dr. William W. Ross, assistant resident in surgery.

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ASSOCIATED FACIAL HEMANGIOMA AND INTRACRANIAL LESION (WEBER-DIMITRI DISEASE)

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AND
MAURICE N. KAY, M.D.
NEW YORK

The syndrome of associated facial hemangioma and intracranial lesion is characterized by the presence of two outstanding signs: (1) a facial port wine nevus (fig. 1) present at birth, which follows the distribution of one or more branches of the fifth cranial nerve, and (2) calcification of the occipital lobe of the cerebrum on the same side as the nevus. This disease has been called after a number of the investigators who have reported cases, including Kalischer,[1] Weber,[2] Krabbe and Dimitri, each of whom was cited by Ford,[3] Brushfield and Wyatt [4] and Sturge, cited by Newson.[5] It has also been referred to as cerebral telangiectasis and, more recently, as associated facial and intracranial hemangioma.

Kalischer was the first to describe the syndrome, in 1897. In 1906 Cushing [6] stated that facial nevi show a tendency to conform in outline to the distribution of one or more branches of the trigeminal nerve and that vascular nevi of the face are associated with lesions of the meninges because of prenatal underdevelopment of the trigeminal nerve. The first

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From the Pediatric Service of Dr. Morris Gleich, Harlem Hospital.

Presented at a meeting of the New York Academy of Medicine (Section of Pediatrics), Nov. 14, 1940.

1. Kalischer, S.: Demonstration des Gehirns eines Kindes mit Teleangiectasie der Linksseitigen Gesichts-Kopfhaut und Hirnoberfläche, Berl. klin. Wchnschr. **48**:1059, 1897.

2. Weber, F. P.: A Note on the Association of Extensive Haemangiomatous Naevus of Skin with Cerebral (Meningeal) Hemanigioma, Especially in Cases of Facial Vascular Naevus with Contralateral Hemiplegia, Proc. Roy. Soc. Med. (Sect. Neurol.) **22**:25, 1929.

3. Ford, F. R.: Diseases of the Nervous System in Infancy, Childhood and Adolescence, Springfield, Ill., Charles C. Thomas, Publisher, 1937, chap. 5, pp. 668-570.

4. Brushfield, T., and Wyatt, W.: Hemiplegia Associated with Extensive Nevus and Mental Defect, Brit. J. Child. Dis. **24**:98 and 209, 1927.

5. Newson, A. L.: A Case of Sturge's Disease, Brit. M. J. **2**:1088, 1939.

6. Cushing, H.: Cases of Spontaneous Intracranial Hemorrhage Associated with Trigeminal Nevi, J. A. M. A. **47**:178 (July 21) 1906.

published report of a case was that of Weber,[7] which appeared in 1922. One year later Dimitri [8] reported a case of angioma of the brain in which a shadow was evident on the roentgenogram. In 1934 Krabbe,[9] a Danish neurologist, reviewed the literature and suggested the name of Weber-Dimitri disease, since these investigators had first published most of the important observations. He collected 5 more cases and reported the results of postmortem examinations, which consisted essentially of cerebral atrophy, a deposition of calcium in the second and third layers of the cortex and destruction of nerve cells in these layers with replacement by neuroglia. He expressed the belief that the cortical lesion was a malformation rather than a calcified angioma. Examinations of the spinal fluid in several of his cases gave normal results. In 1935 Egas Moniz and Almeida Lima,[10] by arteriographic and phlebographic means, showed that no relation was evident between the arterial and the venous circulation and the calcification in the occipital lobe and thereby corroborated Krabbe's observations. In 1936 Greenwald and Koota [11] collected 82 cases of associated facial and intracranial hemangioma. Their series did not include cases of hemangioma of the brain without cutaneous manifestations, because such lesions do not produce signs or symptoms of cerebral disease until the patient is well past puberty and the malformation of the cerebral vessels is usually of the arterial or arteriovenous type.

REPORT OF A CASE

D. W., a 10 year old Negro girl, was admitted to the Harlem Hospital with the complaint of recurrent convulsive seizures during the past four years.

History.—The child was delivered at full term with the aid of forceps after a thirty-six hour labor. The developmental history, both physical and mental, was normal. The child's only illness had been measles, pertussis and mumps. She was well until the age of 6 years, when she had her first convulsive seizure. The mother described the attacks as follows: "The child became unconscious while seated and remained so for five minutes. The eyes were open and staring, and she appeared to be feeling for something with the left hand." The patient

7. Weber, F. P.: Right-Sided Hemi-Hypertrophy Resulting from Right-Sided Congenital Spastic Hemiplegia, J. Neurol. & Psychopath. **3**:134, 1922.

8. Dimitri, V.: Tumor cerebral congenito (angioma cavernosum), Rev. Asoc. méd. argent. **36**:1029, 1923.

9. Krabbe, K. H.: Facial and Meningeal Angiomatosis Associated with Calcification of the Brain Cortex: A Clinical and Anatomopathologic Contribution, Arch. Neurol. & Psychiat. **32**:737 (Oct.) 1934.

10. Egas Moniz and Almeida Lima: Pseudo-angiomes calcifiés du cerveau. Angiome de la face et calcification corticale du cerveau (maladie de Knud H. Krabbe), Rev. neurol. **63**:743, 1935.

11. Greenwald, H. M., and Koota, J.: Associated Facial and Intracranial Hemangiomas, Am. J. Dis. Child. **51**:868 (April) 1936.

stated that she heard talking but could not answer. There was no aura. At first the attacks were infrequent. However, in the six months prior to her first admission they had come on at shorter intervals. The attacks were usually induced by an infection of the upper respiratory tract or by emotional stress. The seizures never occurred in school. On the day of admission the convulsive seizure was generalized, with incontinence of urine and feces. The mother stated that the child was at times difficult to manage and had temper tantrums. During the patient's one month stay in the hospital she had no attacks; however, she was readmitted four months later because of recurrence of the convulsive seizures.

Examination.—The child was well developed and well nourished. She had a port wine stain on the right side of the forehead and the right upper eyelid. The pupils were equal and active. The optic disks and retinas appeared normal.

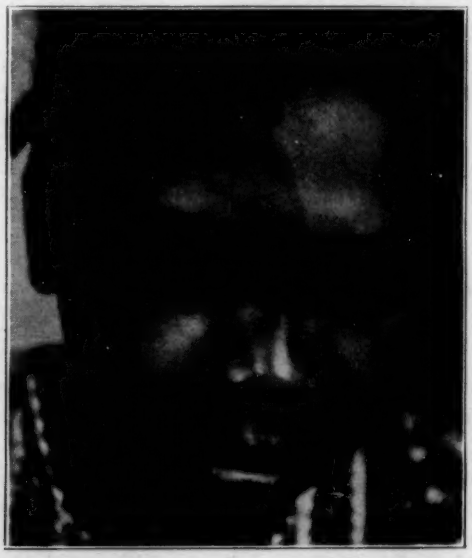

Fig. 1.—Port wine nevus on right side of face, following distribution of branches of right trigeminal nerve.

There were no changes in the corneas and scleras. Examinations of the visual fields revealed left homonymous hemianopia with sparing of the macula lutea, which indicated that the lesion was central and proximal to the optic chiasm. The results of the blindspot studies were normal. There was no evidence of color blindness. The neurologic examination, which was carried out by Dr. R. Gerber, attending neurologist, gave normal results. The child did not appear mentally retarded.

Laboratory Data.—The white cell count was 8,500 per cubic millimeter of blood, with 78 per cent polymorphonuclear cells and 22 per cent lymphocytes. The red cells numbered 4,500,000 per cubic millimeter of blood, and the hemoglobin content was 85 per cent. Examination showed 1.1 mg. of creatinine per hundred cubic centimeters, 13 mg. of urea nitrogen, 82 mg. of sugar, 10.9 mg. of calcium, 4.6 mg. of phosphorus and 10.8 Bodansky units of phosphatase. The reaction to a

Fig. 2.—Roentgenogram of skull, showing the calcified area in the right occipital lobe.

Fig. 3.—Roentgenographic appearance of the cerebral lesion, consisting of a group of double sinuous lines the pattern of which simulates the gyriform surface of the brain.

Kahn test on the blood was negative. Repeated requests for permission to perform a spinal puncture and a pneumoencephalographic examination were refused.

Roentgen and Electroencephalographic Examinations.—The roentgen examination was made by Dr. William Snow. Roentgenograms (figs. 2 and 3), including stereoscopic views, showed a large calcified area in the right occipital lobe which outlined clearly the convolutions of the brain and did not have the appearance of a hemangioma. The electroencephalogram (fig. 4), made by Dr. Hans Strauss, indicated destruction of the occipital portion of the cortex on the right side. The diffuse delta activity over both frontal lobes suggested a convulsive disorder.

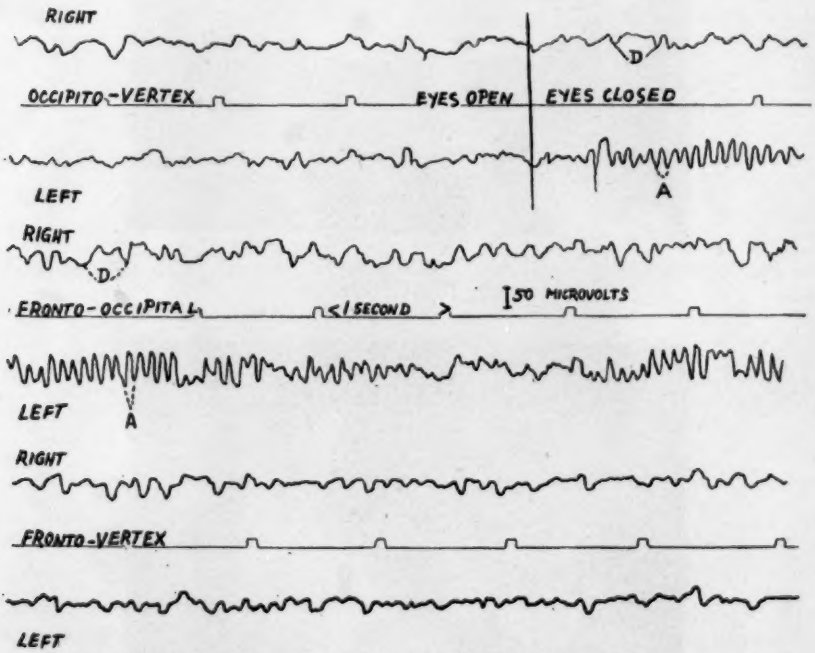

Fig. 4.—Encephalograms. Occipitovertex: same bilateral difference as in the fronto-occipital records. Opening the eyes did not produce any changes in the record obtained from the right side but depressed the alpha activity on the left side.

Fronto-occipital: alpha frequency 11 per second. There was a large amount of alpha activity on the left. On the right there was almost no alpha activity but almost constant delta activity, with frequencies of mostly 4 to 5 per second and amplitudes close to 65 microvolts.

Frontovertex: on both sides, but a little more on the right, there was much delta activity, with frequencies of 3 to 6 per second and amplitudes close to 25 microvolts.

COMMENT

A port wine nevus about the head, neck or face with signs or symptoms referable to the central nervous system should suggest this syndrome even in the absence of the typical roentgenologic evidence. The intra-

cranial lesion has been found both at operation and at necropsy in cases in which there was no roentgen indication of its presence.

In most instances symptoms appear in infancy or early childhood, although they may have their onset in the third or the fourth decade. The first of the symptoms, in order of frequency and importance, is convulsions, which may be general or focal and are frequently the first symptom to appear. The second is paralysis, which practically always involves the side opposite the facial nevus and is usually a hemiplegia; it usually appears shortly after the convulsions, but cases have been reported in which hemiplegia preceded the convulsions by many years. The third symptom, mental retardation varying from slight deficiency to idiocy, was present in about 60 per cent of the cases reported. Other related

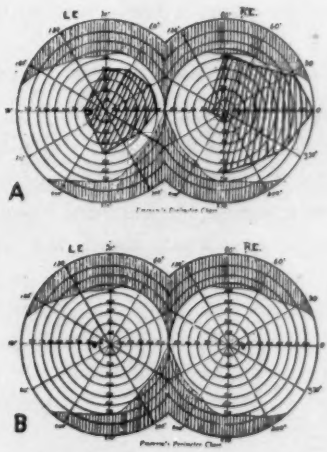

Fig. 5.—Perimeter charts showing, *A*, left homonymous hemianopia and, *B*, normal visual field.

disturbances were faulty memory, temper tantrums, errors in judgment and poor power of concentration. The fourth most common symptom is visual disturbances, of which the following types have been described: homonymous hemianopia, optic atrophy, choked disk, nystagmus, ocular palsies, inequality of the pupils, choroidal atrophy, papillitis, congenital glaucoma and engorgement of the retinal vessels. At least two of the four most important symptoms are present in every case. Other symptoms which have been reported are headache, obesity, deafness, tremors, vertigo and impairment of speech.

Our patient had two of the most common symptoms, convulsions and bilateral left hemianopia (fig. 5). She had no mental retardation but did have temper tantrums.

The roentgenographic appearance of the intracranial lesion is characteristic; the lesion is most frequently located in the region of the occipital pole of the brain. The lesion on the roentgenogram has been described as consisting of sinuous lines, which are often double and which produce a pattern simulating the gyriform surface of the cortex. The opacities are strictly localized to one side, and there is no shadow in the area of the cerebellum. Formerly such shadows were believed to indicate calcium deposits in the walls of the dilated blood vessels or in the meninges, but Krabbe's work seems to indicate that the deposits are actually in the cortex.

The immediate prognosis is good; many patients, however, become mentally defective, and they usually die before middle age.

The treatment of this disease is palliative; high voltage roentgen therapy and operative procedures have been employed to control the convulsions.

SUMMARY

A case is reported of a 10 year old child who had (1) a port wine nevus on the right side of the face, (2) calcification of the occipital lobe of the cerebrum on the same side as the nevus, (3) convulsive seizures involving the side opposite the cerebral lesion, and (4) visual disturbances. Corroborative evidence about the location of the lesion which caused the convulsive disorder was obtained from the electroencephalogram.

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PULMONARY PNEUMATOCELE (BULLOUS EMPHYSEMA)

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The case reported is presented as a typical example of pulmonary pneumatocele following pneumonia in an infant. No attempt is made in this report to discuss the etiologic or the physiologic aspects of cystic disease of the lung. It is believed that proper management in such cases is important for the outcome, and consequently this phase of the subject will be stressed.

REPORT OF A CASE

E. W., a 6 month old white boy, was admitted Jan. 15, 1940, with chief complaints of fever, vomiting and restlessness.

History.—The family history was irrelevant. The baby had been born after a difficult labor lasting thirty-one hours. He was artificially fed; the formula consisted of evaporated milk, corn syrup (Karo), water and lactic acid. The caloric intake was adequate, but the gain in weight was poor. He had had trouble with his ears and also had been treated in another hospital for the same symptoms as those he had on admission.

Part of the information about the present illness was obtained from his case history in the other hospital. Two months after birth the child began to have intermittent attacks of difficult breathing. A roentgenogram of the thymus taken on Aug. 11, 1939, was normal. On September 13 he was admitted to another hospital with gastroenteritis. A roentgenogram of the chest taken September 15, which I examined, revealed something behind the heart. He got along well but pneumonia developed on the left side while he was in the hospital. On September 21 a roentgenogram of the chest revealed fluid. Thoracentesis yielded pus, from which staphylococcus was recovered. On September 26, five days after the tap, a roentgenogram revealed an air bubble behind the heart, and on October 12 a diagnosis of pneumothorax on the left side was made. Roentgen examination after barium was given by mouth ruled out diaphragmatic hernia.

During the next three months a close check was kept on the baby. The "pneumothorax" was tapped on several occasions, with little change in the roentgenographic appearance. On November 11 an infection of the upper respiratory tract developed and he was again admitted to the other hospital, where the "pneumothorax" was again tapped. He was discharged on Jan. 13, 1940 in good condition with the report that the "pneumothorax" was smaller. Manometric readings obtained at the hospital showed a positive pressure of 2 mm. of mercury on inspiration and a negative pressure of 2 mm. of mercury on expiration. Throughout his stay at the other hospital he was never very sick. His tem-

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perature was always below 102 F. Two days after discharge (on January 15) he was admitted to Temple University Hospital with dyspnea and fever.

Physical Examination.—The temperature was 103 F., the respiratory rate 72 and the weight 13 pounds 4½ ounces (6 Kg.). The child was very sick, with dyspnea and an irritating paroxysmal cough. Sudamina, which had been secondarily infected, were observed on the face and neck, and furunculosis of the scalp was present. There were general enlargement of the cervical glands, mild conjunctivitis, purulent rhinitis and some slight redness of the throat.

The chest was tympanitic and the breath sounds were distant over the lower lobe of the left lung, and hyperresonance and exaggeration of the breath sounds were evident over the lower lobe of the right lung. There was impairment to percussion in the right part of the interscapular region, and the breath sounds were tubular and distant. There were fine and medium moist rales throughout

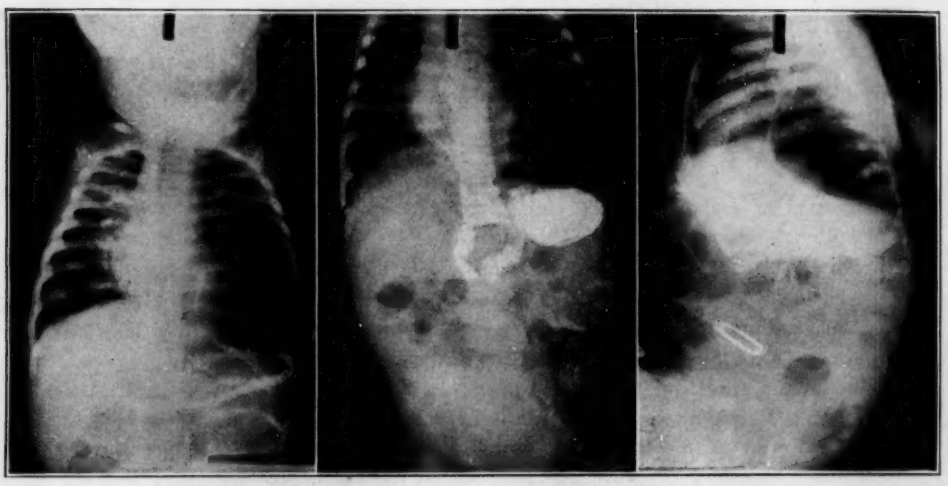

Fig. 1.—Roentgenograms taken Jan. 15, 1940.

the chest. The heart was shifted to the right; the rate was rapid; no murmurs were heard. The abdomen was distended. No masses or organs were palpable. There was marked engorgement of the superficial abdominal veins. The testes were descended, and a hydrocele was present on the left.

Diagnosis on admission was atypical pneumonia associated with pneumothorax or a congenital cyst (fig. 1).

Laboratory Examinations.—The data were of no particular significance in relation to the cystic disease.

Course in the Hospital.—On the day of admission (January 15) sulfapyridine (2-[paraaminobenzenesulfonamido]pyridine) was given in doses of ¾ grain per pound (0.045 Gm. per 0.5 Kg.); on the following day (January 16) sulfamethylthiazole (2-[paraaminobenzenesulfonamido]-4-methylthiazole) replaced sulfapyridine because staphylococci were recovered from the cultures of material from

the nasopharynx. Administration of the drug was continued until January 20, when severe neutropenia necessitated discontinuance. After the drug was stopped the temperature rose again to 103 F., and left otitis media was discovered on January 24. The ear drum ruptured spontaneously. The temperature remained elevated, however, and on January 26 the right ear drum was incised.

On this same day signs of pneumonia in the upper lobe of the right lung were found, and type XIV pneumococcus was isolated. The child was extremely sick and was put into an oxygen tent. He was gvien 40,000 units of antipneumococcus rabbit serum type XIV intravenously, and seven hours later he was given 20,000 units more. Next day his temperature was still 102.5 F. At this time it was thought advisable to institute chemotherapy again. Sulfathiazole (2-[para-aminobenzenesulfonamido]thiazole) was given in a dose of 1 grain per pound

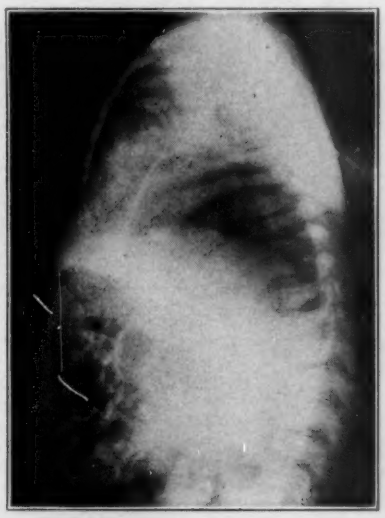

Fig. 2.—Roentgenogram taken Feb. 16, 1940.

(0.06 Gm. per 0.5 Kg.). The temperature fell by lysis, and there was much improvement. Administration of the drug was continued for nine days. (It is interesting to note that the reaction to the Francis test was negative before serum was given, became positive eleven hours after and remained positive.)

On February 12 the child became sick again. Otitis media on the right and bronchitis developed (fig. 2). Since his fever had lasted three days it was decided to try sulfathiazole again. The drug induced a prompt drop in the temperature, but neutropenia developed after it had been given for three days. However, improvement continued, and he was discharged on February 29. At that time the ears were still draining, and coarse rhonchi were present. The collection of air at the base of the left lung seemed unchanged.

Ten days before discharge the collection of air seemed smaller both on physical and on roentgen examination. However, a roentgenogram taken on discharge showed it to be larger than ever.

Readings of Intracystic Pressure.—During the patient's periods of well-being in the hospital manometric readings of the pressure in the cyst were taken. On January 23 the reading was plus 2 mm. on inspiration and plus 6 mm. on expiration; 2 cc. of air escaped during the procedure, and the final reading was 0 on inspiration and plus 4 mm. on expiration. On February 9 the pressure varied between plus 2 and plus 4 mm. on inspiration and between plus 4 and

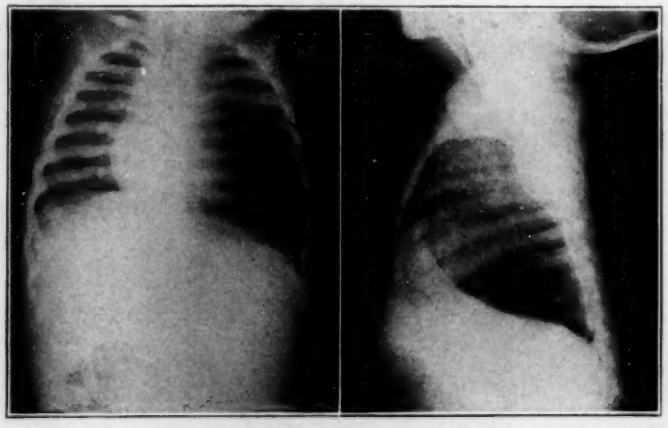

Fig. 3.—Roentgenograms taken April 3, 1940.

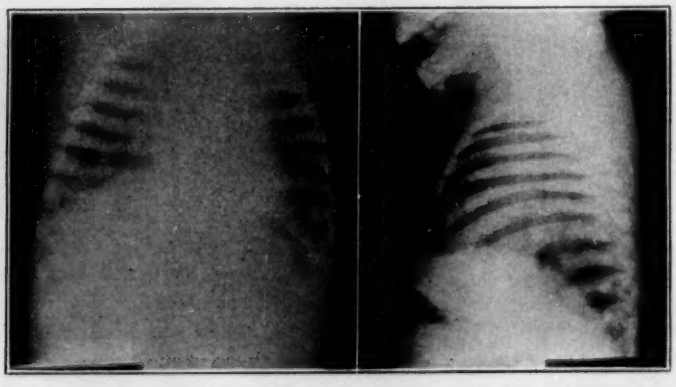

Fig. 4.—Roentgenograms taken June 5, 1940.

plus 10 mm. on expiration. On February 23 the reading on inspiration was plus 2 mm. and on expiration was plus 10 mm.; no air was removed.

Subsequent Course.—After discharge the child got along well, ate well and gained weight. There were no serious complications. He had an occasional attack of bronchitis. The collection of air seemed to remain unchanged (fig. 3). On April 2 he was readmitted so that an attempt might be made to delineate the

cyst by producing an artificial pneumothorax. This procedure was carried out on April 4 and was more or less a failure. The readings of the pressure in the cyst were plus 4 mm. on inspiration and plus 6 mm. on expiration. The readings in the pleural cavity (the needle was in the second left interspace) were minus 2.5 mm. on inspiration and minus 0.5 mm. on expiration. A roentgenogram showed only a minimal collection of air in the left pleural space. The child was discharged and was followed up in the outpatient clinic. He continued to improve and to gain weight, and the wheezing in his chest cleared up (fig. 4). In June 1940 the cyst seemed smaller on physical examination, and the observation was confirmed by roentgen examination. The collection of this air continued to diminish in size from this point on, and by August 1940 (fig. 5) both pulmonary fields were entirely clear on physical and on roentgen examination, and the child was perfectly well.

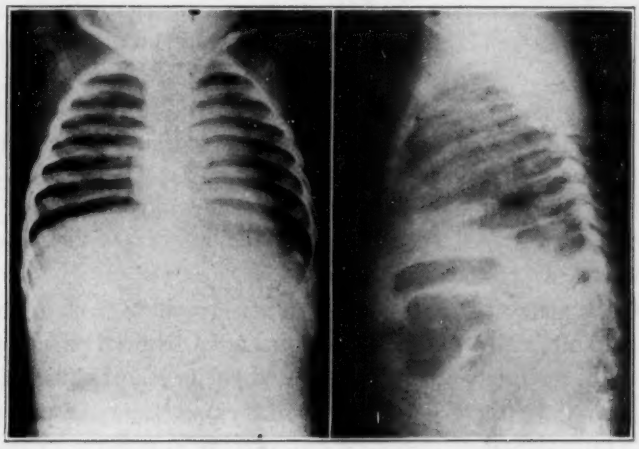

Fig. 5.—Roentgenograms taken July 24, 1940.

COMMENT

There have been many cases of bullae of the lung reported, with various terminations. Croswell and King [1] reported a case in which a solitary air cyst developed after pneumonia in a 3 year old child. The cyst was aspirated several times, but no other surgical measures were employed. It subsided spontaneously. Pierce and Dirkse [2] classified cystic disease of the lung into four main types. The case reported here would fall under their type 4; the probable cause of the disorder of this type was stated to be necrosis of the bronchiolar wall following lobar

1. Croswell, C. V., and King, J. C.: Congenital Air Cyst of the Lung, J. A. M. A. **101**:832 (Sept. 9) 1933.

2. Pierce, C. B., and Dirkse, P. R.: Pulmonary Pneumatocele: Certain Considerations in Cystic Disease of the Lung, Radiology **28**:651 (June) 1937.

pneumonia, with the production of rupture by cough. The authors made no mention of therapy. Willcox and Foster-Carter [3] reported the case of an adult which terminated fatally. The cause of the emphysematous bullae was unknown; rupture caused pneumothorax and death. Gough [4] reported the case of a 29 year old patient in which a bulla ruptured with fatal results. Kaltreider and Fray [5] studied 6 patients with cystic disease of the lung from the physiologic point of view and found a decreased vital capacity and decreased pulmonary reserve. Morse [6] expressed the belief that cystic disease of the lung is probably postpneumonic rather than congenital in origin and cited the case of a 9 year old boy to substantiate this opinion. Benjamin and Childe [7] reviewed the literature of the past six years and discussed the cases of 19 children. In 2 of these cases pneumothorax developed. They expressed the belief that ball valve obstruction of a bronchiole was the cause of the disorder. Caffey [8] has observed 20 patients with the disease, all of whom recovered spontaneously.

In the reported cases of cystic disease of the lung in children little mention is made concerning management. Apparently congenital cystic disease is rare, but it must be kept in mind as a possible diagnosis. On the other hand, acquired cystic disease seems less infrequent and probably goes undiagnosed until spontaneous pneumothorax of nontuberculous origin occurs.

When an air cyst is diagnosed roentgenographically, steps should be instituted to establish a diagnosis by means of an artificial pneumothorax,[2] which will differentiate a tension-loculated pneumothorax from a bullous emphysema. Once the diagnosis of bullous emphysema is established, no active therapy should be instituted unless there is respiratory or cardiac embarrassment from a mediastinal shift. Only then should aspiration be performed. Aspiration may complicate the picture by introducing infection and producing empyema and should not be carried out unless absolutely necessary. Of the 20 patients seen by Caffey,[8] none had the

3. Willcox, A., and Foster-Carter, A. F.: Spontaneous Pneumothorax Associated with Bullous Emphysema, Lancet **2**:315 (Aug. 7) 1937.

4. Gough, J.: Fatal Pneumothorax Due to Rupture of a Solitary Bulla of the Lung, Lancet **2**:314 (Aug. 7) 1937.

5. Kaltreider, N. L., and Fray, W. W.: Pathological Physiology of Pulmonary Cysts and Emphysematous Bullae, Am. J. M. Sc. **197**:62 (Jan.) 1939.

6. Morse, R. W.: Large Intrathoracic Pneumatocele Apparently Secondary to Encapsulated Empyema, Journal-Lancet **60**:87 (Feb.) 1940.

7. Benjamin, B., and Childe, A. E.: Localized Bullous Empysema Associated with Pneumonia in Children, J. Pediat. **15**:621 (Nov.) 1939.

8. Caffey, J.: Personal communication to the author.

disorder for over four months. In the case reported here, the disease lasted about eleven months, and aspiration was never performed during the last seven months of this period. Recovery was spontaneous and complete.

SUMMARY

A case is reported in which bullous emphysema followed pneumonia with empyema. It is believed that in such cases the management should be conservative and aspiration should be done only in the presence of respiratory and cardiac embarrassment.

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JEJUNAL DIVERTICULITIS

ITS OCCURRENCE IN A TWO YEAR OLD GIRL

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Diverticulum of the jejunum, the rarest diverticulum occurring in the gastrointestinal tract, was first described by Sir Astley Cooper [1] in 1844. Case [2] reviewed the literature from 1854 to 1920 and was able to collect only 17 cases in which diverticula of the jejunum and the ileum (other than Meckel's) were found at operation or autopsy. In 1938 Gerster [3] reported 2 new cases and listed 128 references to reports in which 187 cases of jejunal diverticulum were discussed. Since then 32 cases exclusive of the present one have been reported.

Jejunal diverticula may be classified as congenital and acquired. To distinguish between the two types is sometimes difficult. The majority of jejunal diverticula in children are single and congenital, whereas in elderly persons they are usually multiple and acquired. The multiple diverticula usually occur on the mesenteric side of the jejunum, whereas the single diverticula occur on the antimesenteric, as well as on the mesenteric, side. The validity of the distinction drawn between "true" and "false" diverticula on the basis of the number of coats of intestine present has been discounted by many writers. Pathologic specimens have been observed which show not only the "true" and the "false" type diverticula but others which represent transition stages between them.

It is difficult to explain the variability in position of the congenital jejunal diverticulum by assuming that it is a remnant of the omphalomesenteric duct. Lewis and Thyng [4] noted that diverticula or accessory epithelial nodules were present along the course of the esophagus, the stomach and the small intestine in pig, rabbit and human embryos. The majority of such epithelial nodules disappear, but a few persist and give rise to cysts and diverticula.

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1. Cooper, A. P.: The Anatomy and Surgical Treatment of Abdominal Hernia, Philadelphia, Lea & Blanchard, 1844, p. 364.

2. Case, J. T.: Diverticula of Small Intestine, Other Than Meckel's Diverticulum, J. A. M. A. **75**:1463-1470 (Nov. 27) 1920.

3. Gerster, J. C. A.: Ann. Surg. **107**:783-800 (May) 1938.

4. Lewis, F. J., and Thyng, F. W.: Am. J. Anat. **7**:505-519, 1908.

Over seventy years ago Klebs [5] pointed out the weak spots at the mesenteric attachment of the intestine which were due to perforation of the muscular coat at the line of mesenteric attachment by branches of the superior mesenteric artery. In addition to these weak spots, the other factors necessary for the production of acquired diverticula are irregular peristalsis, spasm and increased intra-abdominal distention.

Roentgenographically, a jejunal diverticulum may be recognized as a structure of varying width and length projecting from the barium-filled bowel. The diverticulum may contain barium after the affected segment of bowel is empty, and a fluid level is sometimes seen. The neck of such a sac may be wide or narrow. If the diverticulum contains any non-opaque substance barium may not enter and the sac will not be visualized.

The limitations of roentgenologic diagnosis are well illustrated by the fact that a roentgenogram will frequently not show a jejunal diverticulum which has been seen during an exploratory laparotomy, even when it is particularly examined for the presence of the diverticulum.

Kirklin and Weber [6] of the Mayo Clinic have been able to demonstrate roentgenoscopically various pathologic conditions in the small intestine, such as diverticula (including Meckel's), neoplasms, stenosis, ulcers and tuberculous and nontuberculous ileitis. They have emphasized that examination of the small bowel is essentially a roentgenoscopic procedure and that roentgenograms should be kept for further study and as permanent records.

In most cases the diverticulum gives rise to no symptoms and is discovered accidentally at operation or at autopsy. In children the symptoms may be similar to those of Meckel's diverticulum. Anemia, melena,[7] intestinal obstruction and peritonitis may occur. In older subjects abdominal distention, flatulence and epigastric pain and discomfort are frequent symptoms. Blood in the stools has been noted only occasionally. The more dramatic signs of intestinal obstruction or rupture of the diverticulum, either through trauma or because of an acute inflammatory condition, occasionally occur.

The asymptomatic jejunal diverticulum requires no treatment, and it is unlikely that such an abnormality, adventitiously discovered, will affect the patient's health. There is no effective medical treatment for jejunal diverticulum. Careful attention to the diet, with exclusion of heavy meals, spicy food, large-seeded berries and nuts, has been recom-

5. Klebs, E.: Handbuch der pathologischen Anatomie, Berlin, A. Hirschwald, 1869, vol. 1, p. 271.

6. Kirklin, B. R., and Weber, H. M.: Am. J. Digest. Dis. **7**:475-480 (Nov.) 1940.

7. Normark, A.: Acta pædiat. **20**:475-496, 1938.

mended. A low residue diet has been recommended by some writers, whereas coarse cereals and vegetables have been recommended by others. A diet high in vitamins, particularly the vitamin B complex, is in great favor. Prolonged use of purgatives is inadvisable. If the bowels are sluggish, a mild preparation such as agar is advised.

In the reported cases, surgical intervention was resorted to when there were symptoms of an acute abdominal condition or chronic dyspeptic complaints unrelieved by medical treatment. A single inflamed diverticulum was removed like an appendix. An enteroanastomosis carried out in a case of multiple diverticula with chronic digestive disturbance gave little relief. Jejunal resection was performed in some cases with considerable relief to the patient. Bailey [8] expressed the belief that radical resection of the small intestine is rarely justifiable. He stated that surgical treatment should be limited to those cases in which the condition is resistant to expectant treatment or an abscess, a fistula, threatened peritonitis or an obstruction is demonstrable.

REPORT OF A CASE

M. H., a 2 year old white girl, was admitted to Kingston Avenue Hospital with a history of a polymorphous eruption for one day and vomiting and obstipation of three days' duration. The emesis had become progressively worse, and no feedings were retained on the day preceding admission. Noisy breathing and restlessness had been noted for two days.

The past history was noncontributory.

Examination on admission revealed a poorly developed and nourished child with grunting respirations, sunken eyeballs and temporal fossae, pinched nose and ashy complexion, who retched frequently during the examination. The temperature was 101.4 F., the pulse rate 150, and the respiratory rate 30.

The typical eruption of varicella was present. The turgor of the skin was poor. Examination revealed dulness and bronchovesicular breathing at the base of the right lung, and numerous medium to coarse rales were heard from the apex to the base on the right side. Inspiratory rales were also heard on the left side. The abdomen was markedly distended, with numerous prominent veins running from below upward. There was no definite tenderness, rigidity or masses. Rectal examination gave normal results except that blood-tinged mucus was observed by two different examiners.

The urine was normal. The hemoglobin content of the blood was 80 per cent, and the white cells numbered 18,000, with 81 per cent polymorphonuclears and 19 per cent lymphocytes.

The clinical impression was varicella, pneumonia, dehydration, intestinal obstruction due to intussusception and peritonitis.

Since the patient appeared to be dying, palliative measures were attempted. Gastric lavage, enemas, intravenous administration of physiologic solution of sodium chloride and dextrose and a blood transfusion were given. However, vomiting persisted and distention became more marked.

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8. Bailey, F. W.: S. Clin. North America **18**:1349-1367 (Oct.) 1938.

Surgical intervention was then attempted with the patient under light ether anesthesia. The peritoneal cavity contained a large amount of black fluid, which on culture yielded Streptococcus, Staphylococcus and Bacillus coli. The seat of the trouble was found to be a totally gangrenous diverticulum, the size of an adult finger, which arose from the convex side of the jejunum. The child died before the operation could be completed, less than twenty-four hours after admission.

The pathologist reported that the entire mucosa of the gangrenous diverticulum of the jejunum had been destroyed.

SUMMARY

Two hundred and nineteen cases of jejunal diverticulum have previously been recorded in the literature. A new case, that of a 2 year old girl, in which diverticulitis led to peritonitis and death, is presented.

The occurrence of such diverticula is more frequent than is usually realized. The diagnosis in the past has usually been made during an exploratory operation or postmortem examination. Successful roentgenologic diagnosis has become more frequent in recent years since greater attention and newer technics have been employed in studies on the small intestine.

There are two main types of jejunal diverticula, congenital and acquired. The congenital type is a remnant of an accessory epithelial nodule rather than a vestige of the omphalomesenteric duct. The acquired type is secondary to the combination of points of weakness in the intestine, spasm and increased intra-abdominal distention. Such points of weakness are caused by perforation of the muscular coat of the intestine at the line of mesenteric attachment by branches of the superior mesenteric artery.

The majority of jejunal diverticula give rise to no symptoms, but occasionally they may be the cause of an acute abdominal condition or a chronic digestive disturbance. Blood in the stools is a more frequent symptom in children than in adults. The value of surgical treatment of multiple jejunal diverticula with chronic dyspepsia is disputed. However, there is no effective medical therapy.

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MUSCULAR MACROGLOSSIA

FIVE YEAR OBSERVATION WITH CEPHALOMETRIC AND SPEECH STUDIES IN A CASE OF SPONTANEOUS RESOLUTION

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In 1937 we [1] reported a case of muscular macroglossia and presented an original classification which might serve as a basis for future study. Since that report no other literature has appeared on the subject. In reviewing the literature we were impressed with the lack of follow-up studies. We emphasized that the type of the disorder which we included in our fourth group, that is, idiopathic muscular macroglossia, occurred only in infants and small children and that it was often associated with congenital anomalies of the genitourinary and/or the gastrointestinal tract. Unfortunately, we were unable to obtain roentgenographic visualization of these systems to include in our earlier report because of lack of cooperation.

Surgical excision of a wedge of the tongue was considered for our patient, because it seemed the obvious method of treatment and in several of the reported cases the condition was successfully treated in this manner.[1] However, this was not done because enlargement of the tongue due to idiopathic muscular macroglossia is unknown in adults and older children, which led us to believe that spontaneous resolution might occur. We were of the opinion after completing our report that the child's tongue was definitely getting smaller and that she was able to keep it in her mouth without effort. Further observation confirmed this impression, and now, after five years, we believe that the enlargement has

From the Departments of Pediatrics and Orthodontia, University of Illinois College of Medicine and Dentistry, and the Research and Educational Hospital.

1. Bronstein, I. P.; Abelson, S. M.; Jaffé, R. H., and von Bonin, S.: Macroglossia in Children: Review of Literature; Report of Case of True Muscular Hypertrophy and Suggested Classification, Am. J. Dis. Child. **54**:1328 (Dec.) 1937.

subsided completely. In addition to clinical observation we made studies of the child's subsequent development, especially with regard to her progress in speech attainment and the development and the physical relations of the tongue and the buccal cavity. During our period of observation a number of diagnostic procedures were undertaken in an effort to discover possible associated abnormalities which might be of significance in understanding this unusual deviation from the normal.

CEPHALOMETRIC DATA

In the previous report of this case no data on cephalometric roentgen examinations were included because the difficulty of managing the patient prevented

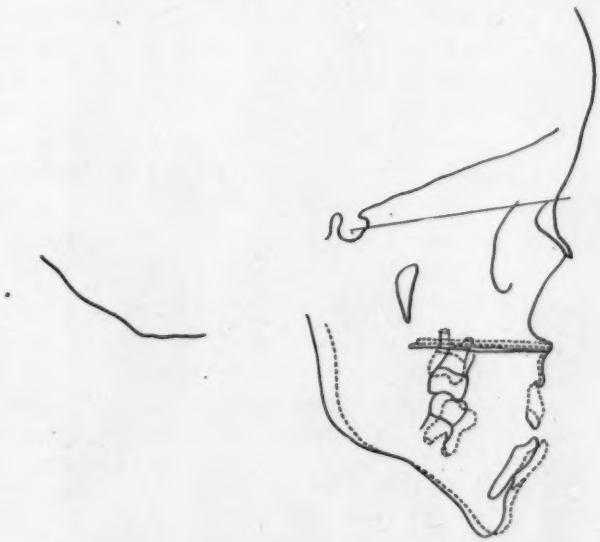

Fig. 1.—Superposed tracings of lateral roentgenograms taken when the patient was 5 years 5½ months (dotted line) and 6 years 5 months (solid line) of age.

our making such examinations. As the age advanced, however, it became feasible to take a series of oriented cephalometric roentgenograms, and these constitute the basis of the present report.

The first and the last of the series were traced and superposed for comparison (fig. 1). It will be noted that there was no change in the cranium, the cranial base or the middle part of the face between the ages of 5½ and 6½ years. In the area below this, however, the dotted and solid lines indicate the amount of change which has occurred. The nasal floor has descended, and the upper alveolar process has gone forward; the upper 6 year molar and the upper incisors have gone down in the normal pattern of growth. The alterations in the mandible indicate more than growth changes, however. Here a discrepancy between the outlines representing the posterior and the lower border of the mandible is seen. The dotted line indicates the size and the position of this bone at the time

the first roentgenogram was taken and the solid line the size and position when the last roentgenogram was taken. A general increase in size is apparent, and this increase corresponds in amount to what might be expected over this interval and at this age. It will be noted, however, that the interval is greater in back than in front and also that the molar and the incisors are posterior to their original position. This can only be interpreted as indicating that the mandible not only has grown normally but has moved backward as well.

Comment.—It is a common clinical observation of orthodontists that the presence of diseased tonsils or any other condition from which escape might be had by a protrusion of the tongue will frequently be accommodated for through a voluntary protrusion of the mandible. This is understandable from an anatomic point of view, since the most anterior points of attachment of the tongue are located at the symphysis. Such protrusion of the mandible brings the condyles out of their fossae, and the patient may assume this position as a comfort accommodation as long as the irritation exists. In the case of the patient under discussion there is no history of irritation, but the retention of the whole tongue within the confines of the jaws would have thrown this organ back into the pharynx. The roentgenograms reveal that during the past year either the tongue has grown smaller or the jaws have increased in size enough not only to accommodate the mass of the tongue but to permit the mandible to go back into its normal relation with the face and the cranium.

RESULTS OF SPEECH EXAMINATION

The patient's past history and the family speech history are essentially noncontributory. The parents speak English fairly well, but with the accent peculiar to Bohemians and Poles. There is no history of speech defect in any ancestor or relative. The speech development of the patient was normal; the first words were recorded at the age of 15 months, and short sentences followed soon after, at the age of 19 months.

Examination revealed a friendly, happy 6 year old girl with a round face. The face was slightly asymmetric, the right cheek being fuller and wider than the left. The facial width between the angles of the mandibles measured 10.5 cm. The corners of the mouth, which was 3.7 cm. wide, drooped slightly and gave the patient the appearance peculiar to a lisper. When the patient was not occupied with talking, laughing or other orificial activity, the normal position of the mouth at rest was slightly agape, with the tip of the tongue protruding and resting on the lower lip. The lower lip was full and the upper thin. In smiling, laughing, crying or talking the upper lip was maintained in a rigid or semirigid position and disclosed sharply demarcated and well developed intermediate and lateral quadratus labii superioris, as well as well developed masseter muscles. Although the maxilla and the mandible approximated, as judged by the teeth level, the lower jaw could not be protruded to project the lower incisors in front of the upper. Similiarly, there was difficulty in retracting the mandible posterior to the maxilla and in opening the mouth widely. No ankylosis of the temporomandibular joint could be demonstrated; the fixity is therefore muscular in origin.

The teeth were regular and even except for the replacement of the inferior central incisors by immature permanent ones, which resulted in a frontal bite of about 5 mm. The gums were normal and healthy. The tongue might be thickened in proportion to the size of the mouth, and although movements were sluggish, they were widely demonstrated in all directions. In speaking the tongue was uncontrollable and projected in needless and undesired positions, which was responsible for some of the speech difficulties.

The palatal arch was low and narrow, as was the pharyngeal orifice. The tonsils were hypertrophied. The nose and ears were essentially normal. The respiration was normal and quiet.

Fig. 2.—The patient, *A*, at 16 months and, *B*, at 4¾ years of age.

The speech was understandable and intelligible. Words were well enunciated and articulated, and the speech was essentially normal except for a lisp, occasional rapid and thereby slurred delivery, occasional lapse into a Polish accent and retention of some infantile traits. "Th" was replaced by "t" or "d," "z" by "s," "r" by "w," final "g" by "k" and "ing" by "unt"; however, all sounds could be imitated correctly except "r." Slurring and infantile speech were demonstrated by the following mispronunciation: 'lil' instead of "little," "mout" for "mouth," "noce" for nose," "lek" for "leg," "fader" for "father." "sewen" for "seven" and "tiwelf" for "twelve"; but "ribbon" was pronounced "wibbon" and "three" "twee."

Comment.—The speech prognosis is good; however, a slight lisp may remain, which will become noticeable with carelessness. A residue of

foreign accent may remain for similar reasons, but notwithstanding these, there will be no difficulty in speech adjustment. This speech attainment is of interest in contrast to that of a child with a partially excised tongue (for a lymphangiomatous swelling) after training and education.[2]

OTHER OBSERVATIONS

We wish to record some brief notes on the subsequent course and development in addition to the results of the special speech and cephalometric studies. Many observations on the height and the weight at various times have shown them to be well within normal limits. On Oct. 20, 1939 the child's height was 42½ inches (77.5 cm.) and her weight 39½ pounds (17.9 Kg.). Two photographs of the patient, showing her healthy appearance, are reproduced in figure 2; *A* was taken when she was 16 months and *B* when she was 4¼ years of age. The child is now 6 years old, is in the first grade of school and appears normal in all respects. She speaks normally except for the remedial defects noted in the special speech examination.

Roentgenograms of the urinary tract obtained by intravenous visualization showed nothing unusual; however, a roentgen examination of the gastrointestinal tract after an opaque meal showed an anomaly of the colon on the left side, consisting of elongation of the sigmoid. This abnormality has not resulted in any functional manifestations, however. The presence of this anomaly fits in with the occurrence of similar malformations of the gastrointestinal tract in the cases reported by other authors.[1] Repeated examinations of the urine and the blood, including creatine studies, showed no deviations from normal. An electrocardiographic study revealed no abnormalities. Measurement of the arms, the legs and the thighs showed complete bilateral symmetry. This procedure was employed to rule out hemihypertrophy, which is frequently associated with muscular macroglossia, as was pointed out in our original communication.

CONCLUSIONS AND SUMMARY

A five year follow-up study of a patient with true muscular macroglossia seems to establish our original conjecture about spontaneous resolution of this anomaly.

The occurrence of resolution, which was suggested by clinical observation, was confirmed by special cephalometric and speech studies.

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2. Bockus, O.: Speech Rehabilitation Following Excision of the Tip of the Tongue, Am. J. Dis. Child. **60**:368 (Aug.) 1940.

AORTIC ATRESIA WITH HYPOPLASIA OF THE LEFT VENTRICLE

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In a series of 1,000 cases of congenital heart disease Abbott [1] included 12 cases in which aortic atresia was the primary lesion and 2 additional cases in which it was associated with another cardiac defect. In 1 of these cases a systolic murmur was noted, in 1 a continuous murmur and in 8 cyanosis. Roberts [2] found 9 cases of this anomaly alone and 6 additional cases in which it was associated with other congenital cardiac defects. He reported another case, that of a second-born twin who had severe cyanosis and dyspnea and who died twenty hours after birth; the first-born twin, who died immediately after birth, had a normal heart. In this group of cases Roberts correlated the duration of life with the size of the interatrial aperture. Three of the same cases were included in a review by Lippincott,[3] who added the report of a case without clinical signs of congenital heart disease to a review of 7 cases from the literature.

REPORT OF A CASE

A white male infant, weighing 8 pounds 7 ounces (3,827 Gm.), was born at Temple University Hospital on Dec. 20, 1940, by spontaneous delivery; it was a vertex presentation, and the labor lasted one hour and twenty minutes. The infant was a second-born child; a sister, 15 months of age, was living and well. The mother, 36 years of age, had been well except for seasonal hay fever and asthma; the pregnancy had been uneventful, and her Wassermann reaction was reported to be negative. The father, 41 years of age, was in good health. The family history was essentially noncontributory.

The baby was cyanotic at birth, and his respirations were irregular. There was only slight improvement after inhalation of oxygen or after crying. The first heart sound was replaced by a long, loud, blowing systolic murmur. There

From the Department of Pediatrics and the Department of Pathology, Temple University School of Medicine.

1. Abbott, M. E.: Atlas of Congenital Cardiac Disease, New York, American Heart Association, 1936.

2. Roberts, J. T.: Case of Congenital Aortic Atresia, with Hypoplasia of Ascending Aorta, Normal Origin of Coronary Arteries, Left Ventricular Hypoplasia and Mitral Stenosis, Am. Heart J. **12**:448 (Oct.) 1936.

3. Lippincott, S. W.: Congenital Atresia of Aortic Valve Without Septal Defect: Report of Case, Am. Heart J. **17**:502 (April) 1939.

was no diastolic murmur and no thrill. The electrocardiogram showed marked right axis deviation.

Oxygen was administered continuously. On the day following birth the murmur was softer and less diffuse and was best heard in the third left interspace. On the second day his condition became worse, without there being any known precipitating factor. The respirations were labored and slightly irregular; the pulmonary fields were aerated. The pulse rate was 120, the heart sounds were of low intensity and the murmur was indistinct. A small amount of mucus, tinged with blood, was obtained by aspiration of the pharynx. The spleen and the liver became enlarged. The extremities were flaccid, cold and mottled; color returned very slowly to an area after pressure. The heart sounds were slightly improved after the subcutaneous injection of caffeine with sodium benzoate. The infant died from cardiac failure on December 23, at the age of 3 days.

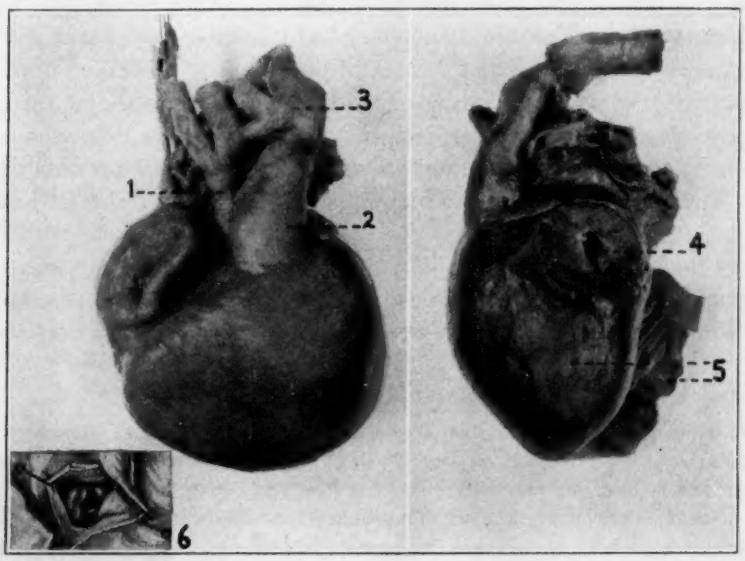


Fig. 1.—Anterior and posterior view of the heart, showing *1*, atresic aorta; *2*, pulmonary artery; *3*, ductus arteriosus; *4*, left ventricle; *5*, right ventricle, and *6*, semilunar valves of the aorta. (In the drawing the semilunar valves are enlarged approximately 3 times.)

Roentgenograms taken immediately after death showed the heart to be approximately twice normal size. It was enlarged in all directions, but the greatest extension was toward the right. The superior portion of the mediastinum was broadened and increased in its anteroposterior diameter, which suggested an enlargement of the thymus; but the trachea, which was displaced posteriorly, was not constricted. No abnormalities were noted in the aerated portions of the lungs.

Autopsy Report.—Autopsy revealed atresia of the aortic orifice and partial atresia of the aorta, enlargement of the pulmonary artery, patent and functional ductus arteriosus, compensatory dilatation of the right ventricle and hypogenesis of the left ventricle and of the left atrium.

The heart weighed 39.5 Gm. (fig. 1). The unusually prominent pulmonary artery measured 1.2 cm. in diameter, as compared with a measurement of 0.8 to

1.0 cm. for that of a normal newborn infant, and the aorta measured only 0.4 cm. in diameter, as compared with the average measurement of 1.0 to 1.2 cm. The right branch of the pulmonary artery originated 0.4 cm. and the left 1.0 cm. above the point of origin of the main pulmonary artery. The left subclavian artery, the left common carotid artery and the innominate artery arose in normal position from the hypoplastic aorta. The coronary arteries arose normally from the aorta. The orifice of the aorta into the left ventricle was not patent, due to a fusion of the valves. The ductus arteriosus was patent. The superior and the inferior vena cava and the pulmonary veins were normal. The right atrium and the right ventricle were enlarged, but the wall of the latter was not thickened. The foramen ovale appeared to be functionally closed. The interventricular septum was normal. The left atrium was hypoplastic. The diameter of the left ventricle was reduced to 0.5 cm., and its wall was moderately hypertrophied.

Microscopically, the myocardium appeared normal. Hematoxylin and eosin, Masson's stain and Verhoff's elastic tissue stain were used in the comparative histologic study of the ascending portion of the aorta, the pulmonary artery and the descending portion of the aorta (figs. 2 and 3). The wall of the pulmonary artery was thickened; the normal elements appeared in correct relation but were proportionately hyperplastic. The thickness of the tunica intima of the atresic portion of the aorta was somewhat reduced but was within normal limits; the media consisted almost entirely of elastic tissue, with practically no collagenous fibers and no smooth muscle cells. No pathologic changes were evident in the wall of the thoracic aorta.

The right lung and the left lung weighed 35 and 30 Gm., respectively. There were areas of partial atelectasis, the majority of which were not congenital. Pneumonia, probably due to aspiration of amniotic fluid, was present. There were multiple small areas of hemorrhage throughout the congested lungs. Careful study of the vessels with special stains did not reveal any abnormal histologic features.

The liver and the spleen were congested; the liver showed fatty metamorphosis; there was a small accessory spleen. The right adrenal gland was larger than the left but otherwise normal. There were small amyloid bodies in the pituitary gland, the significance of which has not been determined.

COMMENT

In this case the presence of a congenital defect of the heart was suspected before death. The nature of the lesion was not determined, but its severity was evident from the clinical course.

One may conjecture concerning the maintenance of life for three days. While the foramen ovale appeared to be functionally closed, it must have allowed sufficient interauricular communication to permit survival for this short period. The patent ductus arteriosus, the murmur of which was elicited, apparently carried the arterial blood from the pulmonary artery to the arteries of the head and the neck and to the coronary arteries. The supply of oxygen to these parts was obviously inadequate. No differential cyanosis of the upper part of the body was noted during life.

The pulmonary artery, which was uniformly hyperplastic, appeared to continue as the aorta. The media of the atresic portion of the aorta

consisted almost entirely of elastic tissue. Careful histologic study of the vessels in the lungs did not reveal any abnormality.

The pathogenesis of the cardiac failure is evident from the pathologic anatomic observations.

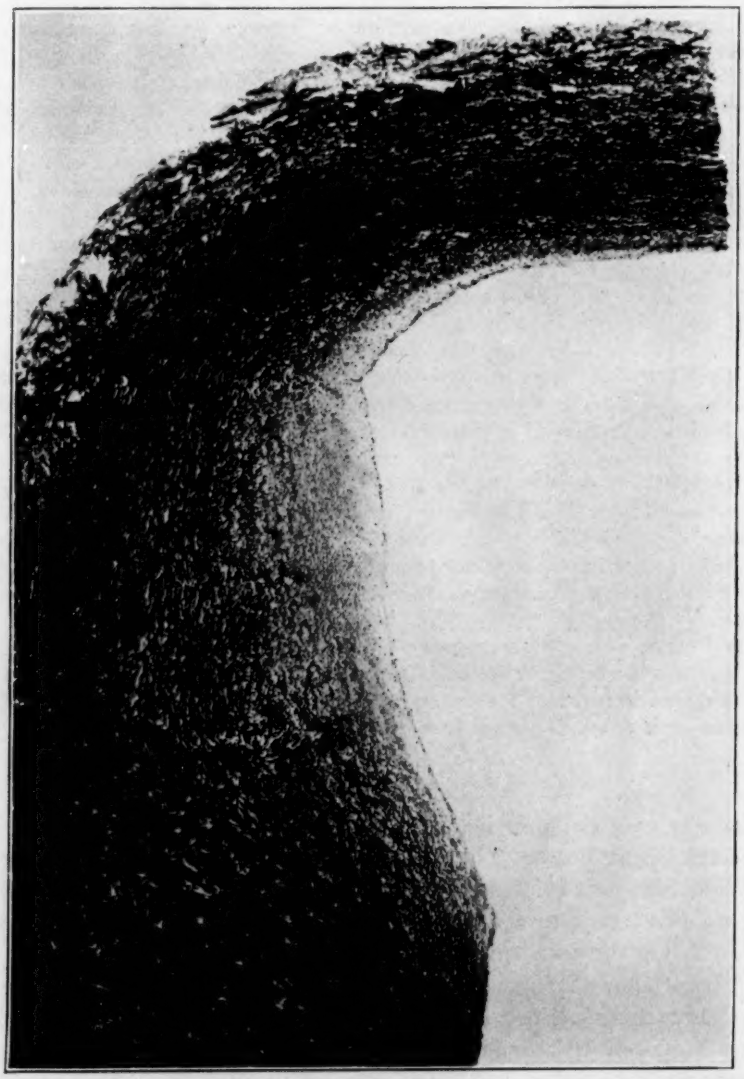


Fig. 2.—Photomicrograph of pulmonary artery; Verhoff's elastic tissue stain; approximately × 30.

SUMMARY

The case of a newborn male infant with aortic atresia and hypoplasia of the left ventricle is reported. There were enlargement of the pul-

monary artery, patent and functional ductus arteriosus and compensatory dilatation of the right side of the heart.

Clinically, the systolic murmur of the patent ductus arteriosus was elicited, and cyanosis was noted. The electrocardiogram showed marked

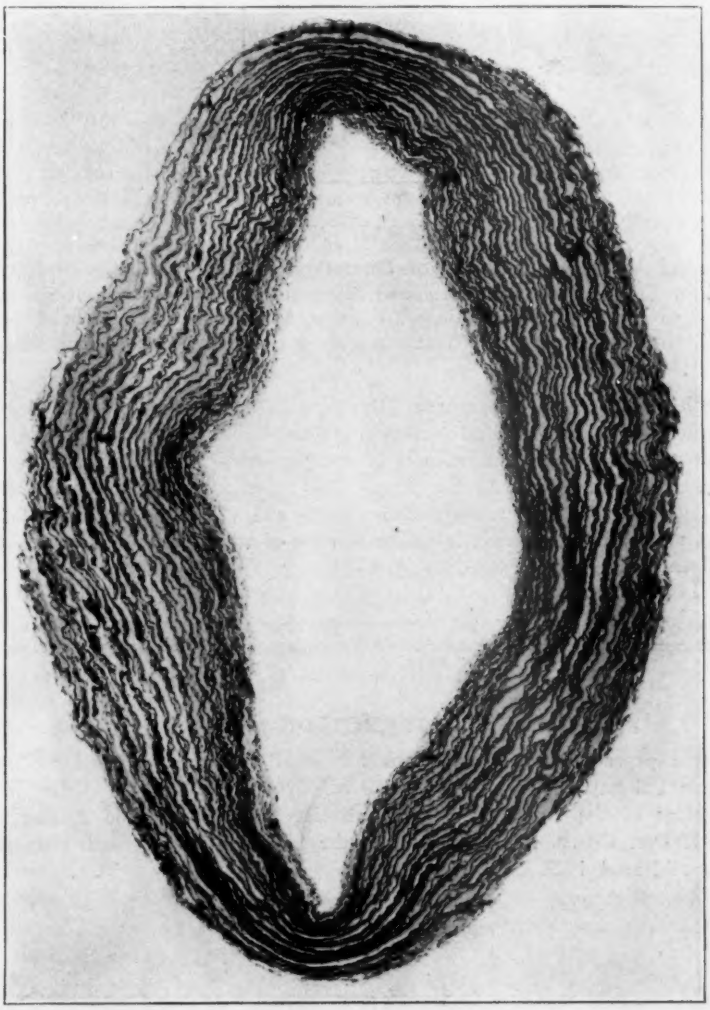


Fig. 3.—Photomicrograph of atresic aorta; Verhoff's elastic tissue stain; approximately × 30.

right axis deviation. The heart was enlarged in all directions, but the greatest extension was to the right.

Death occurred from cardiac failure, three days after birth.

News and Comment

GENERAL NEWS

Second American Congress on Obstetrics and Gynecology.—The Second American Congress on Obstetrics and Gynecology will be held in St. Louis, April 6 to 10, 1942. Preparations are going forward apace, and the Congress should prove to be very important not only for obstetricians and gynecologists but for pediatricians.

Rachford Memorial Lectures.—Dr. Sam Z. Levine, professor of pediatrics of Cornell University Medical College, will deliver the tenth annual series of lectures conducted under the auspices of the Benjamin Knox Rachford Lectureship, in Cincinnati, on Oct. 23 and Oct. 24, 1941. His subject will be "Physiologic Handicaps of Prematurity: Their Pathogenesis and Clinical Applications." The lectures will be held, as usual, in the auditorium of the Children's Hospital Clinic and Research Building.

CORRECTION

In the paper entitled "Spot Maps for Bacillary Dysentery and for Acute Epidemic Poliomyelitis" by Drs. George M. Lyon and Albert M. Price, in the transactions of the American Pediatric Society published in the August issue (AM. J. DIS. CHILD. **62**:437, 1941), in the fourth, fifth and sixth paragraphs 1937 should read 1927.

Abstracts from Current Literature

Anatomy and Physiology

EFFECT OF OXYGEN TENSION OF INSPIRED AIR ON THE RESPIRATORY RESPONSE OF NORMAL SUBJECTS TO CARBON DIOXIDE. NATHAN W. SHOCK and MAYO H. SOLEG, Am. J. Physiol. **130**:777 (Oct.) 1940.

Normal subjects respond with a greater increment in respiratory volume to carbon dioxide (in concentrations of 1, 2, 3 and 4 per cent) mixed with pure oxygen than to the same concentrations of carbon dioxide mixed with air. In some subjects the difference in respiratory response was great enough to be of clinical importance, and this observation should be considered when carbon dioxide is administered for therapeutic purposes. NOURSE, Cleveland.

Biochemistry; Bacteriology, and Pathology

AN INTESTINAL CONTENT CULTIVATION MEDIUM—METHODS OF PREPARATION AND USE—AND DATA OBTAINED IN THE CULTIVATION OF BALANTIDIUM COLI FROM THE PIG. E. CLIFFORD NELSON, Am. J. Trop. Med. **20**:731 (Sept.) 1940.

The author devised a simple method for using intestinal contents in the preparation of a culture medium for the cultivation of protozoa. In his studies the cecal contents of the pig were used in the medium. One part of the intestinal contents was mixed with 9 parts of Ringer's solution and strained through a sieve to remove coarse particles and then through a funnel lined with absorbent cotton.

In this medium strains of Balantidium were cultivated for as long as one hundred and thirteen days. The bacterial growth in this medium is self limited. The protozoa die when the p_H reaches about 5. When the medium was autoclaved to destroy the bacteria the balantidia would not live until a living bacterial population had been established.

He concluded that Balantidium can obtain from the cecal contents all the essentials necessary for growth and multiplication. Also, since serum or host tissue need not be added to the cecal content medium, it seems questionable that Balantidium needs to attack the host. Living bacteria are essential for the growth and multiplication of this organism. BURFEE, Augusta, Ga.

RESORPTION OF ANTIPNEUMOCOCCUS SERUM AFTER INTRAVENOUS, INTRAPERITONEAL AND INTRAMUSCULAR INJECTION. (HOSPITALSTID.) M. BJØRNEBOE and J. CLAUSEN, Nord. med. **1**:906 (March 31) 1939.

Experimental studies were carried out on rabbits with horse and rabbit antipneumococcus serums. If the serum was given by intravenous injection the maximal concentration of antibodies in the blood was found immediately after the injection, if by intraperitoneal injection after three to four hours and if by intramuscular injection after twenty-four to forty-eight hours. A few hours after the injection the antibody concentrations produced by the two first-mentioned modes of injection were almost equal and were notably higher than the concentration achieved by intramuscular injection. A child was given antipneumococcus serum in each of these three ways, and the results of the three procedures were the same. For small children, whose veins cannot be used for injection, the intraperitoneal injection of serum may be used. WALLGREN, Göteborg, Sweden.

Metabolism; Infant Feeding; Milk, and Other Foods

BENZEDRINE [AMPHETAMINE] SULFATE IN OBESITY. GERHARD ROSENTHAL and HARRY A. SOLOMON, Endocrinology **26**:807 (May) 1940.

It was found that amphetamine (benzedrine) sulfate was a useful adjuvant in the treatment of obesity and more effective than thyroid in inducing reduction of weight.

JACOBSON, Buffalo.

ESTIMATION OF THE NUTRITIONAL STATE IN CHILDREN. MANUEL M. GLAZIER, New England J. Med. **222**:180 (Feb. 1) 1940.

The subjects used in this investigation were 556 children between the ages of 2 and 12 years who were followed up from 1933 through 1937. One group was composed of 287 children who attended the first four grades of a primary school in Revere, Mass., and were for the most part from families whose yearly income was between $1,000 and $2,000. Another group included 269 consecutive patients from the outpatient department of the Boston Dispensary, which gives medical service to a section of the population which has a comparatively low income.

One hundred per cent of the children with good nutrition, 92 per cent of those with fair nutrition and 70 per cent of those with malnutrition had good appetites. Study of the amount of sleep required in relation to the state of nutrition and age showed that on the average the children with malnutrition required one hour more sleep daily than those with good nutrition. Seventeen per cent of the children with good nutrition, 40 per cent of those with fair nutrition and 89 per cent of those with malnutrition showed evidence of dietary deficiency or a focus of infection. Twenty-nine per cent showed good nutrition at 2 years and 78 per cent at 13 years of age; the incidence of malnutrition was 50 per cent at 2 years and 9 per cent at 13 years of age. Sixty-six per cent of the children followed a definite familial tendency with regard to height and 34 per cent did not.

Good nutrition, which was least common in early childhood, gradually increased in incidence with age and was commonest in later childhood. Malnutrition, which was commonest in early childhood, occurring among 50 per cent of the children at the age of 2 years, gradually decreased with age until it reached an incidence of 9 per cent at the age of 12 years.

GENGENBACH, Denver.

TREATMENT OF DEHYDRATION. Ö. KERPEL-FRONIUS, Orvosi hetil. **84**:15 (Jan. 13) 1940.

Dehydration may be divided into two types: (1) simple water deficiency and (2) water deficiency combined with salt deficiency. One cannot correct the second type of water deficiency by giving plain water or solutions of dextrose, because if only a small amount of water is given it runs through the organism and if much is given "water poisoning" occurs as a result of the lowering of the osmotic pressure. The most clearcut type of dehydration with salt deficiency is that which occurs after prolonged vomiting. In such cases administration of physiologic solution of sodium chloride has proved quite effective. If the chlorine content of the blood serum is high, it is advisable to add sodium bicarbonate to the physiologic solution of sodium chloride, to avoid acidosis. When the dehydration is too great the plasma exudes from the blood vessels; in such cases transfusions of blood or plasma should be given. If the dehydration is very severe one can expect success only from the use of intravenous infusions, because the solutions given by hypodermoclysis or intraperitoneally are not completely absorbed.

GÖTTCHE, Budapest, Hungary.

ROLE OF THE ADRENAL GLAND IN THE PATHOLOGY OF TOXIC DYSENTERY. S. BLAZSÓ, Orvosi hetil. **84**:164 (March 30) 1940.

In infants with toxic dysentery Blazsó found chemical changes indicative of dysfunction of the adrenal cortex. The histologic examination of the adrenal glands of the children revealed hemorrhage, degeneration and necrosis in the cortex, observations which make justifiable the suspicion that in cases of toxic dysentery the function of the adrenal cortex is disturbed.

GÖTTCHE, Budapest, Hungary.

TEST FOR DETECTION OF COW'S MILK ADDED TO HUMAN MILK. A. GNOSSPELIUS, Svenska läk.-tidning. **36**:2345 (Dec. 22) 1939.

The various methods and reactions which have been used to distinguish mother's milk from cow's milk are discussed and criticized. A new precipitation test is described in which specific rabbit serum is employed. The animals are immunized by repeated injections of cow's milk. The test is performed on a slide and the reaction observed with a microscope. It is possible to detect the presence of as little as 1 Gm. of raw or boiled cow's milk in 100 Gm. of human milk. The reaction is specific and is not influenced by the mother's food.

WALLGREN, Göteborg, Sweden.

Vitamins; Avitaminoses

FUNCTION OF VITAMIN A IN THE MECHANISM OF VISION. M. SIMONELLI, Arch. di ottal. **45**:227 (Sept.-Oct.) 1938.

Simonelli presents a review of the literature on the function of vitamin A in the mechanism of vision. He subscribes to the theories set forth by Wald in his conception of the relation between visual purple and vitamin A.

Simonelli expresses the belief that a measurement of the vitamin A level can be accomplished by means of light adaptation tests. He proposes routine light adaptation tests, especially for children, as a test of the adequacy of the diet.

F. P. GUIDA. [ARCH. OPHTH.]

ENCEPHALOGRAPHY IN RICKETS. G. MURANO, Pediatria **48**:1 (Jan.) 1940.

Lumbar puncture was done on 3 infants, of whom 2 were 3 years and the other 2 years of age. The spinal fluid pressure and chemistry were determined. At the time of puncture 15 cc. of air was injected into the spinal canal, and roentgenograms of the skull were taken after fifteen minutes, thirty minutes and sixty minutes. The author found an increase in pressure and an increase in the amount of spinal fluid. He concludes that there is stasis of the subdural fluid and that this can be interpreted as an early stage of hydrocephalus during the florid period of rickets.

MARTOCCIO, Utica, N. Y.

RICKETS AND OVERCROWDING. B. VEZZOSO, Pediatria **48**:170 (March) 1940.

The author has tried to evaluate the factors which contribute to the incidence of rickets in the various regions of Italy, taking into consideration the overcrowding of homes as an index of poor hygienic and social conditions. He considers as overcrowded those homes in which there are more than 2 persons per room. From his data he concludes that there is a parallelism between the amount of overcrowding and the incidence of rickets in southern Italy. In the other parts of Italy the incidence of rickets is more influenced by climatic conditions (cloudiness).

MARTOCCIO, Utica, N. Y.

HEMATOPOIETIC ACTION OF NICOTINIC ACID. B. VASILE, Pediatria **48**:243 (April) 1940.

The author studied the effect of nicotinic acid on 4 pairs of rabbits. The daily dosage was 3 mg. per kilogram, given subcutaneously. The animals were rendered anemic by bleeding on four consecutive days. The amount of blood removed amounted to one tenth of the body weight. Total and differential blood counts were made daily. The author concludes from his data that the return of the hemoglobin content and the red cell count to normal was more rapid in the animals treated with nicotinic acid. Continuation of the nicotinic acid produced a further increase in the hemoglobin content and the number of red blood cells. Increased polychromatophilia and reticulocytosis were also noted.

MARTOCCIO, Utica, N. Y.

MULTIPLE VITAMIN THERAPY FOR INFANTS WITH DYSTROPHY. E. BONA, Pediatria **48**:260 (April) 1940.

To 10 infants with dystrophy and atrophy the author administered daily 2 teaspoonfuls of a preparation containing amounts of the vitamins equivalent to 5,000 international units of vitamin A, 42.5 units of vitamin B complex, 135 units of vitamin C and 500 units of vitamin D per teaspoonful. After treatment there was an improvement in the general condition, and the weight, the number of red blood cells and the hemoglobin content increased. MARTOCCIO, Utica, N. Y.

USE OF SINGLE MASSIVE DOSES OF VITAMINS IN THE TREATMENT OF RICKETS. J. SCHWARZENBERG L. and JOSE COUSIÑO A., Rev. chilena de pediat. **11**:141 (April) 1940.

This is a monograph of 88 pages in which the effects of massive doses of vitamin D in the treatment of rickets are discussed. The single dose method, granting that the effect is no better than equal to that of current methods of treatment, has the advantages that the physician is sure that the dose is given and the effect is immediately evident. Several preparations of vitamin D, of various potencies, were used, hypodermically and orally. DWYER, Kansas City, Mo.

THERAPEUTIC VALUE OF VITAMIN D_3. ANDREAS NÁDRAI, Arch. f. Kinderh. **116**:235 (April 28) 1939.

Fifty hospitalized infants with rickets in the florid stage were given intramuscular injections of one massive dose of vitamin D_3 (activated 7-dehydrocholesterol) dissolved in oil. Twenty-eight infants received 5, 7.5 or 12.5 mg. of a concentrate of vitamin D_3, and the other 22 infants were given corresponding amounts of a concentrate of vitamin D_2 (calciferol). The healing process of the rickets was examined clinically, by chemical study of the blood and roentgenologically. No difference in the action of the two preparations was noted. Both proved to have an effective antirachitic action. The action of cod liver oil cannot be explained by its content of vitamin D_3. ARON, Chicago.

ROLE OF THE THYROID GLAND IN RICKETS. W. HAASE, Beitr. z. klin. Chir. **168**: 64, 1938.

The experimental work reported was prompted by the results of von Nitschke, who expressed the belief that there is a relation between the function of the thyroid gland and the development of rickets.

The author shows that the feeding of thyroxin according to the plan of von Nitschke does not prevent rickets. Through intraperitoneal injections into animals

of anterior pituitary extracts containing the thyrotropic hormone, there is found definite evidence of functional activity of the thyroid gland in severe rickets.

Rachitic animals show the picture of inactivity of the thyroid glands and animals with healed rickets and those without rickets have active glands. The addition of large amounts of vitamin A to an antirachitic diet does not alter the picture.

RUBIN, Boston.

TREATMENT OF RICKETS WITH ONE LARGE DOSE OF VITAMIN D_2 (CALCIFEROL). J. SZERÉNYI, Orvosi hetil. **84**:24 (Jan. 20) 1940.

Szerényi injected one large dose (15 mg.) of vitamin D_2 (calciferol) in 20 cases of rickets, and quick, complete recovery followed.

GÖTTCHE, Budapest, Hungary.

CLINICAL POINTS OF VIEW ON THE QUESTION OF VITAMIN A. T. LINDQUIST, Nord. med. **2**:1594 (May 27) 1939.

Ninety-three patients with acute pneumonia were examined with regard to their perception of light by means of the photometer of Gullstrand, and determinations of their serum content of vitamin A were made. Hemeralopia was frequent when the content of vitamin A in the serum was 70 international units per hundred cubic centimeters. The level of vitamin A in the serum of patients receiving a rich supply of the vitamin was above 200 international units per hundred cubic centimeters (range, 110 to 400 international units), and none of these patients had hemeralopia. In general, it is rare to find evidence of hypovitaminosis A among persons who have no evident abnormal conditions. Patients with acute pneumonia often have a low content of vitamin A in the serum, which, however, spontaneously increases to normal after the crisis. Administration of large doses of vitamin A to 14 patients with acute pneumonia caused the level of the vitamin in the serum to rise to normal; the death rate among these patients was 0 and among the controls 27 per cent. The use of vitamin A in the treatment of acute pneumonia is therefore recommended. Attention is called to the fact that gross changes in the mucous membranes of the respiratory tract produced by hypovitaminosis A are demonstrable and that the function of the reticuloendothelial system depends, among other things, on the supply of vitamin A. It is probable that infectious diseases are caused by a deficiency of vitamin A. The infection causes a decrease in the vitamin A content of the serum, which may have an unfavorable influence on the course of the disease.

WALLGREN, Göteborg, Sweden.

CLINICAL VALUE OF ASCORBIC ACID AND DIAGNOSIS OF VITAMIN C DEFICIENCY. H. DIFS, Nord. med. **2**:1597 (May 27) 1939.

As an antiscorbutic remedy ascorbic acid is of great value, but whether it has a nonspecific effect on other diseases is questionable. It is not possible to make a reliable diagnosis of hypovitaminosis C by determining the ascorbic acid content of the diet. The capillary resistance test is unreliable; it may give normal results in cases of evident hypovitaminosis C, and there are numerous nondeficiency conditions in which it may give positive results. When the test gives positive results, it must be repeated after a rich supply of ascorbic acid has been administered and may in these circumstances be of some value. It is not proved that the results of saturation tests and determination of the ascorbic acid content of the blood will permit one to make or to exclude the diagnosis of hypovitaminosis C. Individual differences and the effect of combined deficiencies of the diet must be considered in the diagnosis of hypovitaminosis C.

WALLGREN, Göteborg, Sweden.

INHIBITING POWER OF LIQUID PETROLATUM ON THE RESORPTION AND UTILIZATION OF VITAMIN A. T. K. WITH, Nord. med. (Hospitalstid.) **3**:2468 (Aug. 12) 1939.

Experimental studies on rats have shown that when the animals are given carotene dissolved in liquid petrolatum only from one-fortieth to one-fifth as much of the vitamin A is stored in the liver as when the same substance dissolved in a saponifiable oil is given. With large doses of vitamin A the proportion is only one-half. It is supposed that the destruction of carotene and vitamin A in the intestines is accelerated by the presence of liquid petrolatum and that in that way utilization of the substances is inhibited.

WALLGREN, Göteborg, Sweden.

ASCORBIC ACID IN GERMINATING PEAS. H. NATVIG, Nord. med. (Norsk mag. f. lægevidensk.) **2**:1502 (May 20) 1939.

In 1912 Fürst showed that although dry cereals were unable to prevent scurvy they could acquire antiscorbutic properties by being soaked in water and allowed to germinate for one to two days. Using Tillmanns' method, the author tried to determine when the ascorbic acid was formed during the process of germination of peas and the amount of the acid. In dry and also in soaked cereals no ascorbic acid was demonstrable. After a germination of twenty-four hours at 18 Celsius the amount of ascorbic acid produced was about 14 mg. per hundred grams, and the content increased to 40 mg. after a germination of four days. At this time the cereal had a bad odor.

WALLGREN, Göteborg, Sweden.

THE VITAMIN C CONTENT OF HIPS AND THEIR USE AS A SOURCE OF VITAMIN C. H. NATVIG, Tidskr. f. d. norske. lægeforen. **59**:847 (Aug. 5) 1939.

Biologic and chemical examination of hips from different sources and of various stages of ripeness showed that the ascorbic acid content was extremely variable and that this variability depends on the time of harvesting. The highest ascorbic acid content was demonstrated in hips which were picked when they were firm and bright red. The vitamin C is satisfactorily preserved in dried hips. There was practically no decrease in the ascorbic acid content of dried hips between March and November. After one year only 7 per cent less vitamin C was present than when they were fresh.

WALLGREN, GÖTEBORG, Sweden.

INTRACUTANEOUS TEST FOR VITAMIN C. ERIK POULSEN and HERBERT LIECK. Ugesk. f. læger **101**:206 (Feb. 16) 1939.

The authors used the test described by Rotter, in which 0.01 cc. of a solution of 2,6-dichlorophenolindophenol is injected into the skin and the site observed; if decoloration occurs within ten minutes a normal ascorbic acid content of the tissues is indicated, and a delay of more than ten minutes proves that hypovitaminosis C is present. This test was used with 70 per cent for whom the ascorbic acid content of the blood was determined. It was found that the values for different subjects varied so much that the test could not be accepted as a measure of the vitamin C saturation of a subject or as a means of judging the amount of vitamin C present at different times in the same subject.

WALLGREN, Göteborg, Sweden.

AVITAMINOSIS K IN INFANTS AS A CAUSE OF HEMORRHAGIC DIATHESIS. H. DAM, E. TAGE-HANSEN and P. PLUM, Ugesk. f. læger **101**:896 (Aug. 3) 1939.

Thirty-four determinations of the prothrombin content of the blood of normal newborn infants were made; of 22 made during the first week of life, 17 were for infants with icterus neonatorum. Hypoprothrombinemia was present almost constantly during the first week, usually more pronounced during the first days

of life. In addition, 6 newborn infants who suffered from icterus gravis, anemia neonatorum or congenital hydrops (erythroblastosis), with or without signs of hemorrhagic diathesis, and 1 newborn infant who had hemorrhagic diathesis were examined. In all these patients the prothrombin content was decreased, in 6 to a much more marked degree than in normal babies. Injection of vitamin K in 3 cases was followed by a rapid normalization of the prothrombin values and improvement of the hemorrhages. The hypoprothrombinemia of newborn infants is considered to be an expression of an avitaminosis K due to insufficient supply and deficient endogen bacterial production of the vitamin in the intestines. The hypoprothrombinemia produces the hemorrhagic diathesis which is common during the neonatal period.

WALLGREN, Göteborg, Sweden.

CAROTENOID AND VITAMIN A CONTENT OF BREAST MILK. TORBEN K. WITH and CARL FRIDERICHSEN, Ugesk. f. læger **101**:915 (Aug. 10) 1939.

Determinations of the level of carotenoids, by the method of Willstaedt and With (*Ztschr. f. physiol. Chem.* **253**:33, 1938), and of the vitamin A content of the breast milk of 5 healthy women were made every third day for periods of one to three weeks during different seasons of the year. The values varied considerably from day to day (for 1 woman a change from 22 to 40 mg. of carotenoids and from 150 to 445 international units of vitamin A per hundred cubic centimeters was noted) and in different portions of milk obtained during the same day. The variations did not parallel the differences in the amount of milk fat. No definite seasonal variations were observed; the vitamin A content of the diet in winter was 2,350 units and in summer 3,975 units and in addition amounts of carotene equivalent to 1,720 units of vitamin A were ingested. The addition of 3 to 10 mg. of carotene per day to this optimal diet did not produce any evident increase in the amounts of carotene or vitamin A in the milk, although a definite increase in the level of carotene in the serum was demonstrable. The addition of great amounts of vitamin A (120,000 units per day) was followed by an evident increase of the vitamin A content of the milk; in this case no increase in the amount of vitamin A in the serum occurred. Only one third to one fourth of the carotenoids of human milk is in the form of carotene.

WALLGREN, Göteborg, Sweden.

Hygiene; Growth and Nutrition; Public Health

STUDIES IN THE GROWTH AND DEVELOPMENT OF CHILDREN. HARRY BAKWIN and RUTH MORRIS BAKWIN, New York State J. Med. **40**:88 (Jan. 15) 1940.

The factor of age might well be omitted from the Baldwin-Wood age-height-weight table. Height is not a fixed quality but is influenced by environment, as is weight. Proper standards should be based on data for children receiving optimal care. The Bakwin standards are based on the weights and heights of private school children in New York city. Separate standards are necessary for boys, for girls and for colored children. The most suitable standards at present are those based on age and weight and age and height. Optimal care must include paying attention to both psychologic and physical well-being. The psychologic traits of each individual child are different, and knowledge of psychologic growth and development is just as necessary as is knowledge of physical growth and development.

AIKMAN, Rochester, N. Y.

A METHOD OF STUDYING INFANT MORTALITY. LOCKE L. MACKENZIE, New York State J. Med. **40**:886 (June 1) 1940.

This report of the special committee on infant mortality of the Medical Society of the County of New York describes the setup and the methods of procedure for such a committee. The report is presented in the hope that other communities

may be aided in similar projects. Members of the committee are largely obstetricians. Help was secured from the health department, from the municipal hospitals and from the directors of the various obstetric services; junior members of the obstetric staffs acted as representatives. Secretarial service was provided by the New York Maternity Center Association. Studies were made of both stillborn infants and neonatal deaths. A copy of the questionnaire sent out to hospitals and physicians is shown. By the use of this questionnaire the statisticians of the health department were able to make an accurate and helpful study. The conduct of the monthly meetings of the mortality analysis groups is described.

AIKMAN, Rochester, N. Y.

WISCONSIN MARCHES ON. AMY LOUISE HUNTER, Wisconsin M. J. **39**:944 (Nov.) 1940.

Total annual maternal deaths in Wisconsin dropped from 225 in 1932 to 153 in 1939 and total infant deaths from 2,670 to 2,172, even though there was an increase in births. The maternal death rate dropped from 4.2 to 2.8 per thousand live births (a drop of 33.3 per cent), while the infant death rate dropped from 50.0 to 40.1, or 20 per cent, from 1932 to 1939.

Premature babies still acount for the largest number of infant deaths, 36.6 per cent in 1939, 8 per cent higher than the figure for the United States for 1938. Over 99 per cent of the deliveries are by physicians. An appeal is made for more careful supervision during pregnancy, improved care of premature and normal infants and public health education.

JANNEY, Wauwatosa, Wis.

"REFECTORIOS MATERNALES." NOÉ HUAMAN O. Rev. de Hosp. del niño **1**:118 (March) 1940.

A report is given of the splendid results achieved, after three years' trial, with this type of dispensary (modeled after dispensaries in Spain), where groups of mothers are fed and taken care of from the eighth month of pregnancy on and both mother and baby are looked after for six months post partum. Breast feeding is aided by means of balanced diets. There has been a consequent great reduction in the infant mortality rates for the Perú.

JESÚS LOZOYA, Mexico City, Mexico.

Prematurity and Congenital Deformities

CARE OF AND THE MORBIDITY AND MORTALITY RATES FOR THREE HUNDRED AND FIFTY-ONE PREMATURE INFANTS REARED AT HOME. M. GRASSI, Pediatria **48**:90 (Feb.) 1940.

The author concludes that syphilis was the most frequent cause of premature birth among the 351 infants observed. Their growth, morbidity and mortality were directly influenced by the irrational feeding of cow's milk. The principal reasons for stopping breast feeding were ignorance of its proper technic and the poor sucking ability of the premature infant. The hygienic and economic conditions and congenital diseases did not influence the mortality as much as the type of care. The premature infants studied represent 7 per cent of 5,000 infants seen in a clinic. Among the infants 12 per cent were illegitimate and there were 79 sets of twins and 2 sets of triplets.

MARTOCCIO, Utica, N.Y.

FEEDING OF PREMATURE INFANTS. K. SCHWARTZER, Arch. f. Kinderh. **119**:65 (March 8) 1940.

The results of feeding premature infants with human milk alone are not fully satisfactory. A great variety of food mixtures have been recommended for supplementing the human milk. Good results were obtained with citric acid milk

as a supplement. The feeding of citric acid milk was started between the second and the fourth week of life in small amounts, which were increased slowly. From the tenth to the twelfth week of life the infants were usually given the citric acid milk without any addition of human milk. The results of this method are shown in two curves, one for the premature infants whose birth weights were about 820 Gm. and the other for those weighing 1,120 Gm.

The results were improved neither by endocrine therapy nor by feeding additional fluids. Supplements of vitamin B are not regarded as necessary; vitamin C should be given in sufficient quantities. Viosterol in oil or cod liver oil is given when required but not routinely.

ARON, Chicago.

CASE OF ARACHNODACTYLY. S. T. HULTMAN, Nord. med. **1**:610 (March 4) 1939.

The parents and two brothers of a 14 year old boy were healthy and of normal stature. The patient was 56.5 cm. tall at birth and had always been tall and thin for his age. At the time of examination he was 190 cm. tall and weighed 45.3 Kg. His hands, feet, fingers and toes were abnormally long and thin. There were signs of congenital heart disease and bilateral luxation of the lens. The basal metabolic rate was —12 per cent.

WALLGREN, Göteborg, Sweden.

NEUROPATHIC SYMPTOMS IN PREMATURE CHILDREN OF SCHOOL AGE. T. BRANDER, Nord. med. (Finska läk.-sällsk. handl.) **1**:585 (March 4) 1939.

An examination of 376 premature children 7 to 15 years of age was made with regard to psychopathic and neuropathic disorders. In 44 cases there were various kinds of character anomalies and other psychic disturbances. Among the neuropathic symptoms noted in the entire series may be mentioned: enuresis, in 14.5 per cent; pavor nocturnus, in 20 per cent; somnambulism, in 6.1 per cent; encopresis, in 3.5 per cent; finger tremor, in 11.2 per cent; stuttering, in 4.8 per cent, and involuntary movements, in 3.5 per cent. In general there was a greater incidence of pathologic symptoms among premature children of very low birth weight and among children whose parents suffered from oligophrenia, epilepsy, psychosis or alcoholism.

WALLGREN, Göteborg, Sweden.

A CASE OF CEPHALOTHORACOPAGUS. ANTON POULSSON, Nord. med. (Norsk mag. f. lægevidensk.) **1**:310 (Feb. 4) 1939.

In the case reported the esophagus, stomach, duodenum and jejunum were single, while the rest of the intestine and the colon were double; there were two pairs of lungs, arms and legs, two tracheas and one head.

WALLGREN, Göteborg, Sweden.

Newborn

REGARDING ALLERGIC DISEASES OF THE NEWBORN. E. VOGT, Med. Klin. **36**:266 (March 8) 1940.

According to Mayerhofer, allergy in the newborn is produced by sensitization of the fetus during the last days of pregnancy by placental proteins and by maternal sex hormones. Traumatization of the placenta during delivery is assumed to increase this tendency.

The author regards erythema, icterus, melena, mastitis, vaginal hemorrhage, hydrocele, dyspeptic stools and pylorospasm (if present only a few days) as allergic manifestations. He points out that some authors attribute genital bleeding and mastitis to hormonal alteration.

SIEMSEN, Chicago.

A Case of Ophthalmoblennorrhea Neonatorum Gonococcia in which Treatment with Sulfapyridine Was Successful. Mogens Thrane, Ugesk. f. læger **101**:1256 (Oct. 26) 1939.

An infant displayed symptoms of ophthalmoblennorrhea on the fourth day of life. Six 0.15 Gm. doses of sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) were given daily. (A total of 3.6 Gm. was administered). Two days after the beginning of the treatment the eyes were normal.

Wallgren, Göteborg, Sweden.

Acute Contagious Diseases

Experimental Studies on Intraneural Spread of Poliomyelitis Virus. David Bodian and Howard A. Howe, Bull. Johns Hopkins Hosp. **68**:248 (March) 1941.

"It is concluded that: a) The metabolic changes induced in neurones or their axons during the regenerative processes following repeated interruption of the axons by freezing and cutting at least thrice, prevents infection by inoculation of the nerve central to the points of interruption, even when the virus of poliomyelitis is placed in direct contact with every axon. Optimum intervals between successive interruptions of the fiber in the nerve, and the final inoculation, are between two and four weeks, that is, before any considerable number of fibers have completed their regeneration. b) Since the nerve central to the points of interruption is morphologically intact as regards vascular supply, lymphatic connections, connective tissue sheaths, Schwann sheaths, and myelin sheaths, it appears that it is the axis cylinder, as well as the neurone of which it is a part, which is sufficiently altered in its metabolism by the successive distal injuries and the resulting regenerative efforts, to be rendered refractory to the virus. It is therefore highly probable that the axon protoplasm is the active transmitter of the virus in the nerve."

Authors' Summary.

An Outbreak of Scarlet Fever Traced to Raw Milk. Health News **17**:168 (Oct. 7) 1940.

In 6 cases of scarlet fever the cause was traced to a dairy farm, where one of the workers had had a severe sore throat. Examination of one of the cows revealed that a teat dilater had been used and that mastitis due to hemolytic streptococci of the Lancefield group A was present.

Aikman, Rochester, N. Y.

Duration of Diphtheria Immunity: A Follow-Up Study. Amos Christie, J. Pediat. **17**:502 (Oct.) 1940.

The present study is an evaluation of seven different diphtheria antigenic preparations used in the production of diphtheria immunity. Depending on the type of material, amounts given and the period between the injections and the Schick test, 77 to 95 per cent of the infants inoculated were found to have negative reactions to Schick tests in four to twelve weeks. After a four to nine year follow-up period, in 46 to 88 per cent of those with known negative reactions the reactions were found to have continued negative; in 12 to 54 per cent they had reverted to positive. Christie concludes from this study that all children immunized in the first year of life should be given Schick tests again on admission to school. Those giving positive reactions should then receive a stimulating dose of toxoid.

Rauh, Cincinnati.

The Sparing Effect in Poliomyelitis. Gilbert Dalldorf, New York State J. Med. **40**:187 (Feb. 1) 1940.

If monkeys which have been inoculated with a virus of poliomyelitis are given an injection of the virus of lymphocytic choriomeningitis, the first disease

is greatly modified. In the experiments described, a suspension of pooled mixed poliomyelitis virus was given by intracerebral injection. As a rule this produces a fatal result. Of the 16 animals previously inoculated with a virus of lymphocytic choriomeningitis who received such intracerebral injections, 11 recovered. The mortality among the controls was 100 per cent.

If the virus was given after poliomyelitis developed only 30 per cent of the monkeys recovered. The mechanism is not that of cross protection, nor is the result brought about by fever. What bearing these experiments will have on the study of poliomyelitis in man is not known. AIKMAN, Rochester, N. Y.

PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES, FEBRUARY 23-MARCH 22, 1941. Pub. Health Rep. **56**:751 (April 11) 1941.

For the period from Feb. 23, 1941 to March 22 the incidence of measles reached a degree of three and one half times the median number; there were 156,000 cases reported during the four week period. The incidence of pertussis was also 10 per cent over the median. The incidence of all other diseases was below the average. The average mortality rate from all causes was 12.7 per 1,000, which is below average. SANFORD, Chicago.

EXPERIENCE WITH IMMUNIZATION PROCEDURES IN HOME AND OFFICE PRACTICE. F. R. JANNEY, Wisconsin M. J. **39**:599 (Aug.) 1940.

Increase in immunizations by private practitioners and pediatricians depends on their explaining the needs for such action, with the advantages and shortcomings, to the parents while the child is young, before it has become a matter of interest to health departments disposed to immunize. Care in explaining any expected reactions and the protective limitations of each immunization so that there may be no disappointed parents to discredit valuable procedures because of misunderstanding is important.

The need for potent materials always kept well refrigerated needs more consideration.

Sauer's vaccine for pertussis is given first, at about the seventh month, with an additional dose to reenforce the protection later should an exposure occur. Convalescent (or better, hyperimmune) human serum is of value in treatment.

Alum precipitate toxoid, at least two doses, for protection from diphtheria, combined with tetanus toxoid, should be given not earlier than the infant's eighth month of life, and immunity must be checked for at intervals as the years go by.

In smallpox vaccination careful technic is always important to prevent autoinoculation.

Scarlet fever immunization is effective and has a place in private practice, but it is not a clinic procedure; individualization must be had and shortcomings understood by the parents.

Measles modification, especially for debilitated and young children, has value beyond question.

Careful records of all immunizations should be kept, and a permanent record booklet, obtainable from the American Academy of Pediatrics, is most desirable.

JANNEY, Wauwatosa, Wis.

ROSEOLA INFANTUM (EXANTHEM SUBITUM). ROY M. GREENTHAL, Wisconsin M. J. **40**:25 (Jan.) 1941.

The disease was first described in 1910, and the blood picture, with its diagnostic significance, was added in 1921. Roseola infantum, often confused with other exanthems, starts abruptly with high temperature and no abnormal physical findings. There is a relative lymphocytosis. When the temperature drops, more often on the third day, within a few hours a measles-like maculopapular rash occurs, which lasts about two days.

Most obervers consider roseola infantum a clinical entity possibly due to virus.

The author summarizes the salient points in 100 cases observed during the past five years, in which the condition conformed generally to the picture described. Ninety-five per cent of the patients were under 5 years of age. There was no seasonal incidence and no epidemic grouping. Six per cent had initial convulsions, but in general toxic symptoms were lacking. There were no complications. The lymphocytosis in about 70 per cent of the cases is the point most emphasized by the author. JANNEY, Wauwatosa, Wis.

ENCEPHALOMENINGITIS IN MUMPS. MAX J. FOX, Wisconsin M. J. **40**:113 (Feb.) 1941.

Encephalomeningitis as a complication of mumps with recognizable symptoms and signs is not common, but animal experimentation has shown the virus to be present in the spinal fluid in almost all cases of simple parotitis. When the encephalomeningitis does occur the symptom range is much wider than in that of encephalitides in other communicable diseases and the prognosis is more favorable.

The reports of 4 cases are presented. The patients were from 4½ to 7½ years of age, and the onset of the encaphalomeningitis was from three to seven days after mumps. All had fever and headache. Two vomited and 2 had convulsions. All had rigidity of the neck or pain on flexion of the head and other neurologic signs. All were extremely ill but recovered with no sequelae. Examination of the spinal fluid showed markedly increased intracranial pressure in all and cell counts of from 775 to 1,440, with 100 per cent lymphocytes. The sugar content was reduced and the protein slightly elevated. JANNEY, Wauwatosa, Wis.

ENCEPHALITIS COMPLICATING WHOOPING COUGH WITH THE SUBSEQUENT DEVELOPMENT OF EPILEPSY. C. WORSTER-DROUGHT, Brit. J. Child. Dis. **37**:115 (April-June) 1940.

A boy of 5 years had fever and generalized convulsions during the fifth week of an attack of whooping cough. These recurred for a few days. For over five years he was free of attacks and seemed mentally normal. Then the attacks recurred, and he became obese and mentally retarded. LANGMANN, New York.

SUPRARENAL HAEMORRHAGE IN MENINGOCOCCAL SEPTICAEMIA: WATERHOUSE-FRIDERICHSEN SYNDROME. W. H. GRACE, C. V. HARRISON and T. B. DAVIE, Lancet **2**:102 (July 27) 1940.

During a recent epidemic of meningitis there were cases of fulminating hemorrhagic infection in which the patients died within twenty-four hours of onset. There were sudden circulatory collapse and coma.

The so-called Waterhouse-Friderichsen syndrome usually occurs in previously healthy children under 2 years of age but is not limited to children. The patient early shows signs of circulatory failure, with pallor, tachycardia, tachypnea, abdominal pain, vomiting and a petechial or ecchymotic rash.

At autopsy the striking and usually the only pathologic feature of the internal organs, which is responsible for the circulatory collapse, is a massive hemorrhage of the adrenal glands.

Three case reports are appended. LANGMANN, New York.

SIMULTANEOUS IMMUNISATION AGAINST WHOOPING-COUGH AND DIPHTHERIA. HARRY SCHÜTZE, Lancet **2**:192 (Aug. 17) 1940.

Experiments on guinea pigs and rabbits demonstrated the compatability of diphtheria toxoid and pertussis vaccine. The antigenic potency of one did not suffer by the inclusion of the other in the inoculum. LANGMANN, New York.

MILITARY ASPECTS OF ANTIDIPHTHERITIC IMMUNIZATION. F. MEERSSEMAN and M. HULIN, Presse méd. **48**:589 (June 11) 1940.

Diphtheria morbidity in the military population of the fourteenth region of France (about Lyon) was a fraction of that in the civilian population of the same region. Until the injection of toxoid was made universal, this lowering of the morbidity was not achieved. It was found insufficient to use immunization only in military units exposed to diphtheria or for persons with a positive reaction to a Schick test. Ten to 30 per cent of the men showed reactions to the toxoid, but in none were they severe. Renal complications (anuria, hematuria and albuminuria) occurred in 0.1 per cent. Men who had formerly shown albuminuria seemed particularly susceptible to renal complications. Hepatic reactions (characterized by jaundice) are more difficult to evaluate, but these also seemed to occur in subjects with previous histories of hepatic disease. The authors suggest that previous renal or hepatic disease constitute a contraindication for the use of toxoid.

DAFFINEE, Boston.

VITAMIN B_1 IN THE TREATMENT OF POLIOMYELITIS. A. GISMONDI, Pediatria **48**: 48 (Jan.) 1940.

The author treated 11 children suffering from poliomyelitis with injections of thiamine hydrochloride and obtained satisfactory results in all cases. Each cubic centimeter of the preparation used contained 2.5 mg. of thiamine hydrochloride. The average daily dose was 1 cc.

MARTOCCIO, Utica, N. Y.

IMMUNIZATION BY WAY OF THE RESPIRATORY TRACT. G. PETRAGNANI, Pediatria **48**:73 (Feb.) 1940.

The author reviews the results obtained by several investigators in producing immunization by nebulizing diphtheria antitoxin in the air of a room where the subjects were placed. It was shown that the Schick reaction of some of the patients could be made negative. In one group of 59 subjects, the Schick reactions of 56 were rendered negative. Inhalations were given every three days, and the reactions became negative after the eighth inhalation.

MARTOCCIO, Utica, N. Y.

A CASE OF EPIDEMIC CEREBROSPINAL MENINGITIS IN WHICH AIR WAS USED TO BREAK A BLOCK IN THE SPINAL CANAL. F. LUSI, Pediatria **48**:125 (Feb.) 1940.

The author describes the case of a 4 year old child with cerebrospinal meningitis who was treated with intramuscular and intraspinal administrations of serum and with sulfanilamide preparations. Air was injected on two successive days to break a block in the spinal canal. No untoward symptoms were noted. There was complete recovery.

MARTOCCIO, Utica, N. Y.

POSSIBLE RELATION BETWEEN TONSILLECTOMY AND THE INCIDENCE OF ACUTE ANTERIOR POLIOMYELITIS. PIER REMAGGI, Pediatria **48**:184 (March) 1940.

The author examined 582 patients with poliomyelitis, of whom only 3 had undergone tonsillectomy a few months previously. On the other hand, of 224 patients operated on for removal of tonsils and adenoids during a recent epidemic of poliomyelitis, only 1 contracted poliomyelitis, several months after the operation. The author concludes that recent removal of the tonsils and adenoids does not favor an increased incidence of poliomyelitis.

MARTOCCIO, Utica, N. Y.

ROENTGEN STUDY OF WHOOPING COUGH. ANGEL INVALDI and RICARDO PRIG, An. Hosp. de Niños e Inst. de puericultura, 1938, p. 81.

Correlation of clinical and roentgen studies of 120 cases of pertussis with the observations of other investigators led to the following conclusions:

Whooping cough is a pulmonary disease, and in 52.5 per cent of the cases a characteristic localization of the lesion is demonstrable. Early in the course of uncomplicated whooping cough this shadow is a triangular figure with the point toward the vertebral column and the base toward the diaphragm. After the third week, or in whooping cough with complications, many variations in the shadow appear.

DWYER, Kansas City, Mo.

EFFECT OF FLYING IN HIGH ALTITUDES ON CHILDREN WITH WHOOPING COUGH. M. SCHÜTTE, Kinderärztl. Praxis **11**:77 (March) 1940.

Fifteen children suffering from whooping cough were taken up from one to three times in an airplane 9,000 to 10,000 feet (2,700 to 3,000 meters). Each time the plane remained at that altitude for as long as two hours. The results are reported to be encouraging and warrant further trials. Schütte stated that at least 7 children showed marked reduction in severity and frequency of the paroxysms.

HEYMANN, Cleveland.

IMMUNIZATION AGAINST WHOOPING COUGH: I. A CONTROLLED STUDY OF PROPHYLACTIC VACCINATION IN AN ORPHANAGE. FU-T. CHU and JUI-P'ING WU, Chinese M. J. **58**:39 (July) 1940.

The authors have been making studies on the effect of active immunization against pertussis both in human beings and in experimental animals. This report deals with 53 children in a Peiping orphanage. With the exception of 4, all of the vaccinated and control children had been inmates of the orphanage since neonatal days and were known never to have had whooping cough. Thirteen were inoculated with vaccine, and 40 served as controls. These groups lived together. Five months after completion of the vaccination of the 13, pertussis made its appearance in the orphanage. At the outbreak 6 of these were given an additional dose of vaccine (3 cc.) to restimulate antibodies.

None of the vaccinated but 23 of the nonvaccinated group had the disease. Lymphocytosis was found in 10 of the 17 cases in which study of the blood was made; also cough plates in 3 of the 18 cases in which culture was attempted showed Haemophilus pertussis. The serum agglutinin titer for H. pertussis increased during the epidemic in 7 vaccinated children, which indicates that they were exposed. The other 6 children who had been given the additional dose also had an increase in the titer.

NEFF, Kansas City, Mo.

SOME EPIDEMIOLOGICAL OBSERVATIONS ON SCARLET FEVER IN PEIPING. K. I. LI, Chinese M. J. **58**:234 (Aug.) 1940.

Scarlet fever has been endemic in the city of Peiping, and for the years 1931-1932 and 1936-1937 it was epidemic, with the peak in the spring. The highest rate is in the first four years of life, while in America it was found to be at the ages of 5 to 9 years. The fatality is highest in young children, the mortality rate between 18 and 35 per cent. Study of this disease is therefore of great importance, as in the two years when it was epidemic it caused 12 per cent of the annual total deaths. Scarlatina is generally considered to be more common and severe in North China and absent or mild in South China.

NEFF, Kansas City, Mo.

ON THE EPIDEMIOLOGY OF POLIOMYELITIS. E. PETRÉN, Nord. med. **1**:207 (Jan. 27)

The author, who is head of the hospital for epidemic diseases in Malmö, Sweden, expresses the opinion that the poliomyelitis virus, at least temporarily and in crowded communities, is spread ubiquitously and that the disease is communicated by contact with infectious excretions from the upper respiratory tract or from the intestines. In some cases the virus may be spread by milk or by water. The infectious agent is swallowed and enters the body via the intestinal mucosa. Infection usually leads to manifest disease during the enteritis season of the year but may give rise to typical symptoms even during winter and spring. Most persons have good immunizing properties, and that is the reason why infection only exceptionally produces manifest disease. WALLGREN, Göteborg, Sweden.

A NEW INTRACUTANEOUS METHOD OF DIAGNOSING WHOOPING COUGH. F. THURESSON, Nord. med. **2**:1932 (June 24) 1939.

The author has tried an endotoxin produced according to the method indicated by Krueger (*J. Infect. Dis.* **53**:237, 1933). This endotoxin was used in concentrated form and given intracutaneously. The result of the test was read on the third day. A papule measuring at least 3 by 4 mm. was considered a positive reaction. Of 83 children who had not suffered from pertussis, 82 per cent gave negative reactions; of 53 children who had had pertussis, 92 per cent gave positive reactions.

WALLGREN, Göteborg, Sweden.

TREATMENT OF MENINGOCOCCIC MENINGITIS WITH SULFANILAMIDE. GUNNAR NÖRBY, Nord. med. (Hospitalstid.) **2**:1478 (May 20) 1939.

Six children, 3 of whom were 1 year old or less, suffering from meningococcic meningitis were given 10 to 25 cc. of 0.8 per cent aqueous solution of sulfanilamide intraspinally and 50 to 180 cc. intramuscularly. One of the children was dying when admitted to the hospital; the other 5 recovered.

WALLGREN, Göteborg, Sweden.

ACUTE POLIOMYELITIS IN AN INFANT TWENTY DAYS OLD. PAUL ALSÉN, Nord. med. (Hygiea) **1**:871 (March 25) 1939.

The mother of the infant fell ill with acute poliomyelitis one week after delivery. The infant was breast fed. Paralysis of the peroneal nerve of the right side was observed on the twentieth day. Lumbar puncture was not performed. The child recovered but had some residual paralysis.

WALLGREN, Göteborg, Sweden.

PRESENCE OF THE POLIOMYELITIS VIRUS IN LYMPH NODES. C. KLING, G. OLIN and S. GARD, Nord. med. (Hygiea) **1**:929 (March 31) 1939.

In 4 of 33 cases of acute poliomyelitis in children which terminated fatally the poliomyelitis virus was demonstrated in the mesenteric lymph nodes, which were removed aseptically at necropsy. In 1 of 2 cases in which the cervical lymph nodes were examined, the virus was demonstrated. In 11 of the 24 cases in which the spinal cord was examined the virus was present.

WALLGREN, Göteborg, Sweden.

ACUTE INFECTIOUS DISEASES AND HOUSING CONDITIONS. AXEL STRÖM, Nord. med. (Norsk mag. f. lægevidensk.) **2**:1499 (May 20) 1939.

Between 1933 and 1936, 417 cases of diphtheria and 730 cases of scarlet fever were reported in Oslo, Norway. These diseases occurred more frequently in the socially bad districts of the city than in the good districts. The disease occurred

more frequently among persons living in small and crowded flats; 34.9 per cent of the patients with diphtheria and 17.7 per cent of those with scarlet fever lived in overcrowded flats. The average age of the patients decreased with the increase in overcrowding, and the incidence of the contact infections was greater the more crowded the manner in which people lived. WALLGREN, Göteborg, Sweden.

POSTVACCINAL ENCEPHALITIS. PETER M. HOLST, Nord. med. (Norsk mag. f. lægevidensk.) **2**:1505 (May 20) 1939.

In Norway 80 cases of postvaccinal encephalitis have been reported. Fifty per cent of the patients died. In 80 per cent the encephalitis manifested itself on the ninth to the thirteenth day. The author compares the conditions in Sweden and in Norway and calls attention to the fact that in the period from 1933 to 1936 there occurred 1 case of encephalitis per 11,000 vaccinations in Sweden and 1 case per 1,300 vaccinations in Norway. The death rate is greater in Norway than in Sweden (15.5 per cent). As postvaccinal encephalitis still occurs in Norway, the author recommends a discussion of the vaccination question by the authorities.

WALLGREN, Göteborg, Sweden.

FATAL NONSPECIFIC POSTVACCINAL DISEASES. YNGVE ÅKERRÉN, Nord. med. **4**:3554 (Dec. 2) 1939.

The author reports 1 case of meningococcic meningitis developing fifteen days after smallpox vaccination; 1 case of poliomyelitis manifested on the tenth day, and 1 case of acute pneumonia occurring on the seventh day after vaccination. Postmortem examination was done in all cases.

WALLGREN, Göteborg, Sweden.

RHEUMATIC ENDOCARDITIS IN SCARLET FEVER. ARVID WALLGREN, Svenska läk.-tidning. **36**:1015 (May 19) 1939.

Attention is called to the rheumatic genesis in most cases of endocarditis occurring during scarlet fever or shortly after. The rheumatic origin is often demonstrated by concomitant rheumatic signs, such as annular erythema, rheumatic nodules, chorea and a tendency to relapse. Sometimes relapses of previously manifested rheumatic endocarditis may be produced by scarlet fever.

WALLGREN, Göteborg, Sweden.

TREATMENT OF EPIDEMIC CEREBROSPINAL MENINGITIS. C. H. BIE, Tidskr. f. d. norsk. lægefören. **59**:693 (July 1) 1939.

Thirteen cases of meningococcic meningitis are reported in which sulfanilamide, perorally, and specific serum were administered. The first 6 patients received minute doses of the drug, and 3 of them died. The remaining 7 patients were treated with large doses of sulfanilamide and recovered.

WALLGREN, Göteborg, Sweden.

PREVENTION OF DIPHTHERIA. KNUD BOJLÉN, Ugesk. f. læger **101**:59 (Jan. 19) 1939.

Bojlén expresses the opinion that the epidemiologic importance of the diphtheria endemic in Copenhagen is underrated. It is necessary to combat the infection with energy. There exist two means by which to fight the spread of diphtheria: isolation of carriers of the bacillus and preventive vaccination with the anatoxin of Ramón. The first method is considered useless and expensive. The latter method is recommended as being effective, easily employed and much less expensive.

WALLGREN, Göteborg, Sweden.

EPIDEMIC OF MILK-BORNE SCARLET FEVER AND TONSILLITIS. E. JUEL HENNINGSEN and J. ERNST, Ugesk. f. læger **101**:298 (March 9) 1939.

One hundred and eighteen cases of scarlet fever and 50 cases of tonsillitis occurred within a few days in a community of 25,000 inhabitants. The epidemic could be traced to a milkmaid of the dairy from which the patients had obtained milk. The maid suffered from purulent otitis (Streptococcus pyogenes, group A, type 3). The virus could be cultivated from the patients. The milk was repeatedly examined, with negative results. The epidemic ceased rapidly after pasteurization of the milk.

WALLGREN, Göteborg, Sweden.

POSTVACCINAL ENCEPHALITIS. A. ELDAHL, Ugesk. f. læger **101**:938 (Aug. 10) 1939.

A girl of 6 years fell ill with encephalitis on the twelfth day after smallpox vaccination and died on the third day after the onset. The diagnosis was confirmed at postmortem examination.

WALLGREN, Göteborg, Sweden.

Acute Infectious Diseases

A FAMILY OUTBREAK OF PNEUMOCOCCUS TYPE I INFECTIONS. NORMAN PLUMMER and HERBERT K. ENSWORTH, Am. J. M. Sc. **201**:100 (Jan.) 1941.

An outbreak of infections, which included an infection of the upper respiratory tract in 3 persons, pneumonia in 1 and a gastrointestinal upset in 1, in a family of 5, all of whom were shown to harbor type I pneumococci in the nasopharynx, is reported.

The apparent transfer of the organism to a sister's family with the subsequent outbreak of an infection of the upper respiratory tract in 1 member and a type I pneumonia in another is described.

Before boarding out a child from a home where there is a case of pneumonia, a throat culture which is negative for the type of pneumococcus causing the patient's illness is recommended.

HENSKE, Omaha.

INFECTIOUS MONONUCLEOSIS—A DIAGNOSTIC PROBLEM. SAMUEL J. WERLIN, VERA B. DOLGOPOL and MORRIS E. STERN, Am. J. M. Sc. **201**:474 (April) 1941.

"1. Patients with infectious mononucleosis often are severely ill. An extensive pharyngitis is usually present, often simulating diphtheria.

"2. Cervical lymphadenopathy in early infectious mononucleosis may occasionally simulate mumps.

"3. Early differentiation of infectious mononucleosis from diphtheria is desirable in order to avoid unnecessary administration of diphtheria antitoxin and sensitization of the patient to horse serum.

"4. Cases of clinical diphtheria which do not respond to antitoxin must be investigated hematologically and serologically for the possibility of infectious mononucleosis.

"5. Non-toxic diphtheria-like bacilli may be present in the nose and throat of patients with infectious mononucleosis.

"6. In children the highest white blood counts are observed during the first week of illness, in adults in the second week of illness.

"7. The heterophil antibody reaction was positive in 90% of 21 patients of this series.

"8. The titer of sera showing positive heterophil antibody reactions remains constant for months, if the sera are stored in an icebox. Positive sera may be used as control in performing the test with unknown sera."

AUTHORS' CONCLUSIONS.

CEREBRAL CHANGES IN ROCKY MOUNTAIN SPOTTED FEVER. GEORGE B. HASSIN, Arch. Neurol. & Psychiat. **44**:1290 (Dec.) 1940.

An 11 year old white girl was bitten by a tick on a farm near Peoria, Ill. She complained of headache and vomited. Six days after she was bitten her hands and feet were covered with a rash and she became comatose. She died eleven days after being bitten. A brother of the patient, who also became sick after a tick bite, recovered. The author draws the following conclusions:

"1. The histologic changes of the central nervous system in Rocky Mountain spotted fever are those of nonsuppurative meningoencephalitis.

"2. The encephalitis is histologically analogous to the type produced by typhus fever and other forms of severe encephalitis.

"3. Although on the basis of histologic studies of the central nervous system a diagnosis of this disease is not decisive, one may assume with certainty that in Rocky Mountain spotted fever the central nervous system is fundamentally involved."

BEVERLY, Chicago.

TOXIN-ANTITOXIN REACTIONS IN EXPERIMENTAL TETANUS. H. B. SHUMACKER JR., W. M. FIROR and A. LAMOT, Bull. Johns Hopkins Hosp. **67**:92 (Aug.) 1940.

"1. When tetanus antitoxin is injected intravenously into guinea-pigs, mice, dogs and cats a given amount of antitoxin does not neutralize the same number of guinea-pig median lethal doses of toxin in each species. The number of G-P LD50's that are neutralized is least in the very sensitive guinea-pig, greater in the slightly less sensitive mouse, and still greater in the resistant dog and cat. This difference cannot be explained either by the difference in the lethal dosage for each species or by a difference in concentration of antitoxin.

"2. Regardless of the species used, there are differences in the protecting power of intravenously injected antitoxin against toxin subsequently introduced by various routes. Antitoxin is only very slightly effectual against toxin placed in the spinal cord; is very much more effectual against toxin given intradermally, intramuscularly, or subcutaneously; and is still more effectual against toxin injected intravenously. Antitoxin is most effectual when mixed in vitro with the toxin and then injected into the animal.

"3. The experimental results are discussed in relation to certain theories proposed in the literature."

AUTHORS' SUMMARY.

BLACKWATER FEVER (HEMOGLOBINURIA) CAUSED BY SPIDER BITE. HENRY B. GOTTEN and J. J. MACGOWAN, J. A. M. A. **114**:1547 (April 20) 1940.

A 3 year old girl was bitten by a brown spider, probably not of the black widow type, in a southern state. She had fever, toxemia, anemia and coal black urine due to hemoglobinuria.

The causes of hemoglobinuria (besides malaria) are listed as quinine, phenol, aminoacetic acid intoxication, transfusion of blood from an incompatible donor, severe toxemia due to burns or infections and exposure to extreme cold. In some cases the symptom is paroxysmal. This report adds another possible cause to the list.

HEERSMA, Kalamazoo, Mich.

HEMATOLOGIC INDEX OF THE MECHANISM OF THE ACTION OF ANTIMONY AND POTASSIUM TARTRATE IN THE THERAPY OF INTERNAL LEISHMANIASIS. F. VECCHIO, Pediatria **47**:1026 (Dec.) 1939.

The complete blood counts for 6 patients who were treated with antimony and potassium tartrate are given. A 1 per cent solution in double distilled water was used. Three of the patients were under 2 years and 3 were over 4 years of age.

MARTOCCIO, Utica, N. Y.

PURULENT MENINGITIS CAUSED BY THE TYPHOID BACILLUS. R. CANNATA, Pediatria **48**:59 (Jan.) 1940.

The author reports the case of a 5 year old child who had a high fever and diarrhea for two months. At the end of this time retraction of the head and marked headache appeared. Lumbar puncture yielded a cloudy fluid under increased pressure which showed typhoid bacilli on culture. At autopsy ulcers of the ileum, mesenteric adenitis and purulent meningitis were observed. This case was reported because of the rarity of the disease.

MARTOCCIO, Utica, N. Y.

COMPLEMENT-FIXATION POWER OF THE BLOOD SERUM IN LEISHMANIASIS INTERNA. G. MURANO, Pediatria **48**:83 (Feb.) 1940.

The author determined the complement-fixating power of the blood serum of 12 infants with leishmaniasis interna and of 8 normal infants. There was noted a marked increase in the complement-fixating power of the serum of those with leishmaniasis. This complement-fixating power cannot be used to evaluate the defensive capacity of the body.

MARTOCCIO, Utica, N. Y.

LATENT MALARIA REVEALED IN THE COURSE OF ACUTE INFECTIOUS DISEASES. R. CANNATA, Pediatria **48**:113 (Feb.) 1940.

Cases in which a malarial infection which has been latent until the onset of another infectious disease appears are not common. The author reports 1 case of typhoid and 1 of cerebrospinal meningitis in which characteristic febrile attacks occurred and malarial parasites were found.

MARTOCCIO, Utica, N. Y.

ANOTHER CASE OF TYPHOID ENCEPHALITIS. H. G. HUBER, Kinderärztl. Praxis **11**:11 (Jan.) 1940.

A case of severe encephalitis with typhoid fever is described. There was complete recovery in this 13 year old girl, as there had been also in an 11 year old girl whose case was described previously (*Kinderärztl. Praxis* **8**:152, 1937). Huber stated the belief that the intravenous injection of 40 cc. of a 35 per cent solution of dextrose on alternate days was beneficial.

HEYMANN, Cleveland.

IMPORTANCE OF OXYURIASIS AND TREATMENT WITH LUBISAN-BAYER. H.-C. HEMPEL, Kinderärztl. Praxis **11**:149 (May) 1940.

In some regions of Germany from 70 to 90 per cent of the children of school age are infected with Oxyuris vermicularis. Inspection of the rectum two hours after a child has been in bed for the night, when the worms are visible at the anus, is of greater diagnostic reliability than the finding of the ova in the feces or of eosinophils in the blood. Lubisan, which Hempel recommends for treatment, is a derivative of resorcinol (resorcinolmonobutyl ether diethylcarbamate). It is only slightly toxic. A group of 272 children was subjected to a three day treatment in the following way:

The evening before the first day of treatment supper was omitted. On the morning of the first day breakfast was delayed until three hours after the dose of lubisan had been given. The dose varied from 0.3 to 0.9 Gm. according to the age and weight of the child. No other meals were given on the first day. On the morning of the second day of treatment the fasting dose was repeated and was followed three hours later by 2 to 3 tablespoonfuls of castor oil. After the first bowel movement the first meal of the second day was given. Supper was omitted. Treatment on the third day was the same as on the second day. Repetition of the first day's treatment is recommended three weeks later, for one day. Complete cure was obtained in about 90 per cent of the children treated. Reinfection

was avoided by treatment of all infected members of the family, by application of unguentum cinereum externally to the rectum of the patient and by having the patient wear at night bathing trunks which were boiled daily.

HEYMANN, Cleveland.

TREATMENT OF UNDULANT FEVER TREATED WITH SULFANILAMIDE. MOGENS JERSILD, Ugesk. f. læger **101**:756 (June 22) 1939.

Three cases of undulant fever (one that of a girl 11 years of age) in which treatment with sulfanilamide was successful are reported.

WALLGREN, Göteborg, Sweden.

Chronic Infectious Diseases

THE VALUE OF TUBERCULIN SKIN TESTS IN PEDIATRIC PRACTICE. PAUL W. BEAVEN, New York State J. Med. **40**:466 (April 1) 1940.

Tuberculin cutaneous tests have a definite place in private practice and should be used regularly by all physicians practicing among children. They not only show whether the subject has a primary infection but also help to detect sources of infection. Beaven gives a complete review of the literature. In a discussion, H. F. Rowley reported the result of tests of 769 infants and children in private practice, in which 15 positive reactions were obtained. Of the 15 children, only 3 had a family history of the disease. Four showed roentgenographic evidence of tuberculosis.

AIKMAN, Rochester, N. Y.

LET US WASSERMANNIZE THE EXPECTANT FATHER. MELVYN BERLIND, New York State J. Med. **40**:885 (June 1) 1940.

In the state of New York compulsory Wassermann tests are required of expectant mothers. These tests are not necessarily made at the first examination. Berlind states that a negative Wassermann reaction during pregnancy does not rule out syphilis and that a syphilitic child may be delivered from an apparently healthy woman with a negative Wassermann reaction. He mentions 3 cases in all of which tests of the blood of the husbands gave positive reactions. He recommended that a routine Wassermann test be required of the expectant father.

AIKMAN, Rochester, N. Y.

FAMILIAL VULNERABILITY OF SPECIAL SITES TOWARDS THE LESIONS OF CONGENITAL SYPHILIS: ISCHEMIC DISTURBANCE IN FINGERS OF TWO SISTERS, PROBABLY DUE TO THIRD GENERATION SYPHILIS. T. ANWYL-DAVIES, DAVID NABARRO and F. PARKES WEBER, Brit. J. Child. Dis. **37**:173 (July-Sept.) 1940.

The mother of the 2 girls was known to have latent untreated syphilis (probably congenital). Both girls had signs of "commencing gangrene" of the fourth and fifth terminal digits of the right hand soon after birth. The elder child's condition gradually healed with scarring, and the Wassermann and Kahn reactions were negative. The younger child was seen during the active stage of the condition, and her serologic reactions were positive.

LANGMANN, New York.

A CASE OF CONGENITAL TUBERCULOSIS. J. J. GOURNAY and MARC REGNARD, Paris méd. **1**:65 (Feb. 3-10) 1940.

On Feb. 27, 1939 a boy was born prematurely, at 7½ months, of a mother with active tuberculosis. He was isolated from the mother immediately and had no contact with any other tuberculous person. The placenta appeared normal, and the tuberculin reaction of the baby was negative. Physical examination revealed no

abnormality. He did well until April 11, when he had fever. A week later he became dyspneic and rales were heard in the upper lobe of the right lung. On May 3 the tuberculin reaction was positive. Meningitis developed, and death occurred on May 23. Autopsy revealed miliary tuberculosis, tuberculous meningitis and areas of caseous pneumonia. LESLIE, Evanston, Ill.

ANERGIC TUBERCULOSIS. H. OPITZ, Kinderärztl. Praxis **11**:1 (Jan.) 1940.

Three cases of tuberculous adenitis are described. Scrofula was present in 1 patient, who gave a negative reaction to an intracutaneous tuberculin test. All 3 patients were tested repeatedly with 0.01, 0.1, 1 and 10 mg. of tuberculin. The state of anergy could not be explained either by the history or by the physical examination. The diagnosis was established by examination of a biopsy specimen from the lymph nodes and by finding the bacilli in stomach washings. The conclusion given is that a negative reaction to tuberculin should not inhibit further investigation to establish a diagnosis of tuberculosis. HEYMANN, Cleveland.

TUBERCULOSIS IN CHILDREN IN SHANGHAI. C. L. KAO, Chinese M. J. **58**:113 (July) 1940.

Since 1934, when a survey was reported, tuberculin tests have been given to school children and to those children coming to the clinic who showed evidences of nutritional disturbances or illness. Tables are given of the results of Mantoux tests in primary schools, in the outpatient department of the Children's Hospital and in two groups of children with reference to social status. Combined results of these tests show that of 5,393 children up to 14 years of age who were given the tests 3,313 (61.4 per cent) had positive reactions.

Other tables include the results of tuberculin tests and roentgenographic changes in the chests of 648 infected infants and older children. A practical scheme of preventive treatment is outlined for those primary school children in whom tuberculin tests elicit positive reactions. NEFF, Kansas City, Mo.

DEMENTIA PARALYTICA INFANTILIS ET JUVENILIS. GEORG K. STÜRUP, Ugesk. f. læger **101**:245 (Feb. 23) 1939.

Two cases are reported of dementia paralytica in girls 14 years of age whose mothers had positive Wassermann reactions. The symptoms began when the children were about 10 years of age, with backwardness in school and "nervousness." Examination some years later displayed dementia, abnormal pupillary reflexes and positive Wassermann reactions in the blood and in the spinal fluid. The cell count of the spinal fluid was respectively 20 and 42 per cubic millimeter. Both girls were given malaria and antisyphilitic treatment, without success. The author emphasizes the importance of early diagnosis and early treatment.

WALLGREN, Göteborg, Sweden.

Diseases of Blood, Heart and Blood Vessels and Spleen

CHLOROSIS: ESSENTIAL JUVENILE IRON DEFICIENCY ANEMIA. GUNNAR ALSTED, Am. J. M. Sc. **201**:1 (Jan.) 1941.

Having studied the cases recorded the author concludes that chlorosis has not, as generally assumed, entirely disappeared but that it does still occur, even if with comparative infrequency. Diagnostic criteria remain the same as ever: hypochromic iron deficiency anemia without any demonstrable cause occurring in young women with a normal gastric function. The disease seems to be more common in older women than formerly. The term chlorosis has covered an anemic condition in young girls shortly after puberty. It might be better to use the term essential

juvenile iron deficiency anemia instead of chlorosis. In this way the disease is kept distinct from simple achylic anemia, for although the two diseases show a certain pathogenetic relation, they must still be regarded as separate entities.

HENSKE, Omaha.

THE SICKLING PHENOMENON, WITH SPECIAL REFERENCE TO THE DIFFERENTIATION OF SICKLE CELL ANEMIA FROM THE SICKLE CELL TRAIT. I. J. SHERMAN, Bull. Johns Hopkins Hosp. **67**:309 (Nov.) 1940.

"Increased leukocyte concentration, temperature elevation, and bacterial contamination have each been found to accelerate sickling, while saline dilution and increased oxyhemoglobin concentration have been found to retard the occurrence of sickling in sealed standing preparations. This furnishes an explanation of the inconsistency of results obtainable with this method, and also supports the theory that sickling in these preparations is brought about by the lowering of the oxygen tension due to metabolic activity.

"The basic rôle of oxygen tension in the sickling phenomenon and the reversibility of this phenomenon has been demonstrated.

"It has been found that certain fixatives do not alter significantly the amount of sickling in cell suspensions.

"A new morphologic reaction of the erythrocyte which is capable of sickling has been described. It has not been observed in normal erythrocytes.

"A difference between sickle cell anemia and the sickle cell trait with regard to the oxygen tension at which sickling will occur has been reported.

"Sickle cells have been found regularly in high percentages in the venous circulation of patients with sickle cell anemia, but this has not been found in the peripheral circulation of patients with the sickle cell trait.

"In patients with sickle cell anemia, sickle cells have been found in higher percentages in the venous circulation than in the arterial circulation.

"A method has been described which furnishes a rapid test for sickle cell anemia, differentiating it from the sickle cell trait." AUTHOR'S SUMMARY.

ERYTHROBLASTIC ANEMIA. F. R. B. ATKINSON, Brit. J. Child. Dis. **37**:89 (April-June) 1940.

This article consists of a short summary of the historical background and of the pathologic, clinical, hematologic and roentgenologic aspects of this disease. An extensive bibliography is appended. LANGMANN, New York.

STUDIES ON STORED BLOOD: IV. MODIFICATIONS IN THE EQUIPMENT FOR BLOOD TRANSFUSIONS. C. P. STEWART, Edinburgh M. J. **47**:571 (Aug.) 1940.

The author pictures and details two types of apparatus for blood transfusion which he has devised. The second one is more convenient, more easily sterilized and portable. The flask in which the citrate solution has been sterilized is hooked up and utilized as part of the transfusion apparatus, making it unnecessary to transfer the solution from this flask to another container.

NEFF, Kansas City, Mo.

TIME RELATIONS OF HEPARIN ACTION ON BLOOD-CLOTTING AND PLATELET AGGLUTINATION. D. Y. SOLANDT and C. H. BEST, Lancet **1**:1042 (June 8) 1940.

Experimental work with dogs suggested that even the most extensive injury to arteries or veins never results in a maximal stimulus to platelet agglutination. The findings suggest that in the presence of even a little heparin an effect on agglutination previously produced by a higher concentration may persist.

LANGMANN, New York.

SYNTHETIC VITAMIN K IN TREATMENT OF HYPOPROTHROMBINAEMIA. ROBERT KARK and ALEXANDER W. SOUTER, Lancet **1**:1149 (June 29) 1940.

A group of 18 patients with hypoprothrobinemia were treated parenterally with a water-soluble derivative of 2 methyl-1, 4 naphthoquinone (menadione). In 9 the lowered prothrombin concentration in the blood was rapidly restored to normal level. In 3 patients with hemorrhage the bleeding was satisfactorily controlled. Twelve patients with hypoprothrombinemia associated with parenchymatous hepatic disease did not respond to intensive parenteral administration of either the water-soluble synthetic vitamin K or natural vitamin K obtained from alfalfa.

LANGMANN, New York.

CAPILLARY FRAGILITY. G. H. BELL, S. LAZARUS and H. N. MUNRO, Lancet **2**:155 (Aug. 10) 1940.

The fragility of the capillaries of the skin of the antecubital fossa was examined by Göthlin's method in a series of 346 healthy British students. A 300 watt lamp at a distance of 2 feet (61 cm.) was used as the illuminant. A pressure of 50 mm. of mercury was maintained for fifteen minutes.

Petechial counts of under 8 were found in 89.3 per cent of cases. In most cases in which the count was 8 or over the ingestion of vitamin C reduced the count to less than 8 in two weeks.

Apart from abnormal influences, e. g., fever and administration of heavy metals, two factors influence capillary fragility in health: menstruation and ascorbic acid. This study suggests that other factors are involved.

LANGMANN, New York.

SURVIVAL OF STORED RED CELLS AFTER TRANSFUSION. S. R. M. BUSHBY, A. KEKWICK, H. L. MARRIOTT and L. E. H. WHITBY, Lancet **2**:414 (Oct. 5) 1940.

When blood is collected in a 3 per cent solution of sodium citrate in the proportion of 100 cc. of the citrate solution to 440 cc. of blood and stored at 4 to 6 C., the following procedures prolong the period of preservation of the red cells, as judged by a quantitative fragility test: adjustment of p_H to 5, dilution and the addition of dextrose.

LANGMANN, New York.

A HAEMORRHAGIC DIATHESIS IN IDIOPATHIC STEATORRHOEA: OBSERVATIONS ON ITS ASSOCIATION WITH VITAMIN K DEFICIENCY. ROBERT KARK, ALEXANDER W. SOUTER and JOSEPH C. HAYWARD, Quart. J. Med. **9**:247 (Oct.) 1940.

The authors describe the case of a 62 year old white man with idiopathic steatorrhea. He had been treated with a low fat diet for two and one-half years, and a severe hemorrhagic tendency had developed, with marked hypoprothrombinemia. This was corrected by the oral administration of synthetic vitamin K (menadione).

Similar cases described in the literature are reviewed.

BRADFORD, Rochester, N. Y.

PAROXYSMAL TACHYCARDIA IN A NEWBORN INFANT. NILS LINDQUIST, Nord. med. **4**:3556 (Dec. 2) 1939.

A boy with congenital heart disease suffered from several attacks of tachycardia (maximum heart rate, 214) and signs of decompensation (cyanosis, dilatation of the heart and enlargement of the liver). The crisis lasted several hours to one day. During the free intervals the heart rate was 130 to 150. The child was last seen when he was 7 months old. The electrocardiogram showed a negative P wave; in other respects it was normal.

WALLGREN, Göteborg, Sweden.

Diseases of the Nose, Throat and Ear

TREATMENT OF UPPER RESPIRATORY TRACT INFECTIONS IN CHILDREN. H. K. TENNEY, Wisconsin M. J. **39**:816 (Oct.) 1940.

Simple practical points in the care of respiratory infections are mentioned. Extra rest is most important whether obtained by putting the child to bed or otherwise. In the early stages of the "drizzly nose" antiseptic nose drops are of benefit, and in the later stages, when there is a thick discharge, vasoconstrictor drops, steam and suction are valuable. The technic of administering nose drops is more important than the kind of drops used. The head should be definitely low; otherwise the drops merely moisten the floor of the nose as they go back into the nasopharynx. Acetylsalicylic acid is valuable for malaise. The intake of food is usually automatically controlled by the child. For infants cough mixtures should be simple and conservative.

The ears should be carefully examined, as otitis may develop silently, and changes in the appearance of the drum are more important than inflammation, as is the presence of pulsation. It is rarely wise to open an ear during the first few hours of involvement, even if there is bulging. Sulfanilamide and its derivatives are recommended if there is aural involvement.

For croup, steam inhalations, hot compresses and hot drinks are used, while antipyrine is almost specific.

In tonsillitis, even with grave constitutional reactions, there is rarely the complaint of pain, which further emphasizes the need for a thorough physical examination.

JANNEY, Wauwatosa, Wis.

PREVENTION OF MASTOIDITIS. V. G. HORAN and S. GAY FRENCH, Lancet **1**:680 (April 13) 1940.

A series of 621 cases in which acute suppurative otitis media was treated with sulfanilamide is reported. The incidence of mastoiditis was only 3.4 per cent, as compared with 22.7 per cent before the introduction of this drug. No serious toxic manifestations were seen.

LANGMANN, New York.

LARYNGEAL OBSTRUCTION IN CHILDHOOD. F. ARDEN, M. J. Australia **2**:331 (Oct. 12) 1940.

Arden describes the following various conditions which cause laryngeal obstruction in children: (1) congenital laryngeal stridor, which is due to the presence of an unusually flexible epiglottis, the lateral margins of which are rolled backward so that they almost meet posteriorly (the aryepiglottic folds are thus brought close together, which gives the entrance to the larynx the appearance of being pinched from side to side; the condition disappears spontaneously during the second year as the larynx enlarges and its walls stiffen); (2) laryngismus stridulus (never seen in Brisbane); (3) foreign bodies in the larynx; (4) papilloma of the larynx (rare and tends to retrogress at puberty); (5) stenosis of the larynx; (6) acute catarrhal laryngitis; (7) laryngitis stridulosa (children with this condition [croup] in early life not infrequently have asthma later); (8) syphilitic laryngitis; (9) edema of the glottis; (10) retropharyngeal abscess; (11) acute laryngotracheobronchitis, and (12) laryngeal diphtheria, which is still the commonest cause.

When an artificial airway must be provided tracheotomy is preferable to intubation.

GONCE, Madison, Wis.

THREE CASES OF BRONCHOSTENOSIS. GERT VON SYDOW, Nord. med. **2**:1224 (April 22) 1939.

The first case was that of a girl 1½ years of age in whom bronchostenosis with emphysema of the left lung was demonstrated after an infection of the upper respiratory tract. The bronchostenosis did not produce the least deterioration of

the girl's general state of health, although it had been present for at least five months. In the 2 other cases the bronchostenosis had been caused by tuberculosis of the bronchial glands.

WALLGREN, Göteborg, Sweden.

CASE OF CONGENITAL LARYNGEAL STRIDOR. S. SIWE, Nord. med. **2**:1225 (April 22) 1939.

A child 1½ years of age had suffered from distinct laryngeal stridor since birth. It varied in intensity. There were abnormal mobility and laxity of the epiglottic cartilage; at every inspiration the epiglottis displaced itself horizontally over the laryngeal introitus. The possibility of dysplasia of the epiglottic cartilage is discussed.

WALLGREN, Göteborg, Sweden.

Diseases of Lungs, Pleura and Mediastinum

SULFATHIAZOLE IN THE TREATMENT OF PNEUMONIA IN INFANTS AND CHILDREN. ALBERT V. STOESSER and ROBERT MOONEY, Am. J. M. Sc. **201**:718 (May) 1941.

Seventy-seven infants and children admitted to the pediatric service of the Minneapolis General Hospital from January to July 1940 with a diagnosis of pneumonia were given sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole).

"Various doses of the sulfathiazole were tried and in doing this all ages of the children were fairly well represented.

"The response to the sulfathiazole therapy was most encouraging. There was little of the nausea and vomiting frequently encountered with sulfapyridine. . . . The most disturbing feature of the chemotherapy was the appearance of a drop in the polymorphonuclear blood cells. With discontinuance of the drug the white blood cells soon returned to the normal figure.

"Careful clinical observations of the patients receiving the various amounts of the sulfathiazole together with the determinations of the level of the drug in the free state in the blood permitted a dosage schedule to be established. It is presented with the understanding that although this will be of value to the practicing physician at the present time, future clinical studies may produce changes which will give even better results."

HENSKE, Omaha.

CURRENT BRONCHOPNEUMONIA OF UNUSUAL CHARACTER AND UNDETERMINED ETIOLOGY. YALE KNEELAND JR. and HANS F. SMETANA, Bull. Johns Hopkins Hosp. **67**:229 (Oct.) 1940.

The authors report 52 cases of atypical bronchopneumonia observed in the past two years at Presbyterian Hospital, New York. The main clinical features are as follows: The course of the infection is characterized by an insidious onset. The leukocyte count is normal or only moderately elevated. The sputum bacteriologically is such as might be obtained from healthy persons at that time of year. Pulmonary consolidation is migratory. In many of the cases the disease is mild.

Chemotherapy had no effect on the course of the disease.

In 1 case with fatal termination the lesion in the lung was characterized by a mononuclear cellular exudate and an acute pulmonary vasculitis.

LYTTLE, New York.

BRONCHOPNEUMONIA OF UNKNOWN ETIOLOGY (VARIETY X): A REPORT OF THIRTY-TWO CASES WITH TWO DEATHS. WARFIELD T. LONGCOPE, Bull. Johns Hopkins Hosp. **67**:268 (Oct.) 1940.

The author describes 32 cases of an unusual type of bronchopneumonia, the clinical characteristics of which seem sufficiently well defined to allow one to recognize it as a clinical entity. The clinical picture is similar to that described

in the article by Kneeland and Smetana (*Bull. Johns Hopkins Hosp.* **67**:229 [Oct.] 1940). The cause is unknown, but it has been suggested repeatedly that the disease is caused by some sort of virus.

LYTTLE, New York.

SULFATHIAZOLE IN THE TREATMENT OF PNEUMONIA IN INFANTS AND CHILDREN: A REPORT ON 167 PATIENTS TREATED WITH SULFATHIAZOLE AND A COMPARISON WITH 93 PATIENTS TREATED WITH SULFAPYRIDINE. JOHN P. SCOTT and ALBERT M. JONES, J. Pediat. **17**:423 (Oct.) 1940.

One hundred and sixty-seven patients with pneumonia were treated with sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole), the dosage being based on the body weight. In all but a few cases a daily dose of 1 grain (0.065 Gm.) per pound of body weight was used. In 146 of the cases, the condition was thought to be lobar pneumonia; in 19 it was bronchopneumonia, and in 2 the diagnosis was uncertain. One hundred and sixty-two of the patients recovered and 5 died. All the deaths occurred in infants under 1 year of age. Pleural effusions occurred in 7 patients. One patient, whose condition was complicated by pleural effusion, died and was found to have multiple staphylococcic pulmonary abscesses. Operation for empyema was necessary in 1 case in which sulfathiazole was ineffective and type XXXI antipneumococcic serum was given. In 1 case sulfathiazole was ineffective and type VI serum was used with success. In another case in which sulfathiazole was ineffective sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) was used with success. In 3 cases sulfathiazole was effective in causing the pleural exudate to resolve. Catarrhal otitis media occurred in 56 cases and resolved without drainage. In 31 cases the otitis was suppurative but responded well to treatment.

"Toxic effects were largely gastrointestinal . . . and were mild in comparison to similar effects caused by sulfapyridine.

"Sulfathiazole is equally as effective as sulfapyridine in producing critical falls in temperature in patients with pneumonia."

RAUH, Cincinnati.

SPONTANEOUS PNEUMOTHORAX AND STAPHYLOCOCCAL LUNG ABSCESS. J. LEIGH COLLIS and A. F. FOSTER-CARTER, Lancet **1**:875 (May 11) 1940.

A case is described of spontaneous pneumothorax in an infant aged 8 weeks. Necropsy revealed that this was due to the rupture of a staphylococcic abscess of the lung. The roentgenographic appearances were strikingly similar to those of a pulmonary cyst. It appears from the literature that a pyogenic pulmonary infection is the commonest cause of spontaneous pneumothorax in infants under 1 year of age.

LANGMANN, New York.

CINEBRONCHOGRAPHY (CINEMATOGRAPHY THROUGH THE BRONCHOSCOPE). JOHN E. G. MCGIBBON, Lancet **1**:1083 (June 15) 1940.

The author describes an apparatus by means of which he has successfully produced films depicting in motion the normal appearance and movements of the larynx, trachea and larger bronchi, together with some of their commoner abnormalities as seen through the bronchoscope.

LANGMANN, New York.

SULPHATHIAZOLE IN THE TREATMENT OF PNEUMOCOCCAL LOBAR PNEUMONIA. WILFRED F. GAISFORD and WILLIAM WHITELAW, Lancet **2**:451 (Oct. 12) 1940.

Ten patients with lobar pneumonia (pneumococcic) were treated with sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole). The results showed that the drug acts similarly to sulfapyridine. It produces a less prompt fall in temperature, and there is a correspondingly longer period of acute illness. The chief

point in its favor is that it does not cause vomiting. The authors have used sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) for the initial dose and sulfathiazole for the subsequent doses and have obviated vomiting in this way.

LANGMANN, New York.

TREATMENT OF PNEUMONIA WITH SULPHAPYRIDINE AND SERUM. THOMAS ANDERSON and JOHN G. CAIRNS, Lancet **2**:499 (Oct. 12) 1940.

Of 217 patients with infections due to pneumococci of types I, II and III, 197 were treated with sulfapyridine alone and 20 with sulfapyridine and serum.

The fatality rates (excluding deaths within twenty-four hours) for patients treated with the drug only were as follows: 0 per cent for those with type I infection, 6.6 per cent for those with type II infection and 23 per cent for those with type III infection. Only patients with type II infections were treated with both the drug and the serum, and for these the fatality rate was 5 per cent. The fatality rate for patients with bacteremia was at least double that for those without bacteremia whose pneumonia was due to the same type of bacillus.

LANGMANN, New York.

ATYPICAL SILENT PNEUMONIA COMPLICATED BY BILATERAL OTITIS MEDIA. E. HURMUZACHE and SEBASTIAN PINELES, Bull. Soc. de pédiat. de Iasi **10**:50, 1939.

A child aged 18 months after a slight cold suddenly had a high temperature, with morning remissions to 37.4 C. (99.3 F.). Bilateral otitis media was found, but there was no improvement following paracentesis. Physical examination otherwise gave negative results, but roentgen ray examination revealed consolidation of the middle lobe of the right lung.

LESLIE, Evanston, Ill.

TWO CASES OF SPONTANEOUS PNEUMOTHORAX OF NONTUBERCULOUS ORIGIN IN INFANTS. E. HURMUZACHE and S. PINELES, Bull. Soc. de pédiat. de Iasi **10**:59, 1939.

The cases of 2 infants 11 months of age are reported. The first was well developed and well nourished. The Wassermann and Mantoux reactions were negative. During the course of bronchopneumonia she became suddenly extremely agitated and the temperature which had been high dropped to 37 C. (98.6 F.) and remained there. Roentgen ray examination showed a collapsed left lung with a mediastinal shift to the right. The baby was discharged from the hospital three days later in apparent good health but with the same roentgen ray picture. In the second child the pneumothorax followed a rather typical lobar pneumonia. The resorption of air with expansion of the lung was accomplished in thirteen days. This child had a positive reaction to a Mantoux test but had received B C G vaccine at birth.

LESLIE, Evanston, Ill.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

THE COMPLICATIONS OF MECKEL'S DIVERTICULUM IN INFANCY AND CHILDHOOD, WITH AN ANALYSIS OF FOURTEEN CASES. MERRILL W. EVERHART, J. Pediat. **17**:483 (Oct.) 1940.

Fourteen cases of Meckel's diverticulum are presented. They fall into two groups, 5 cases of the inflammatory type with perforation and 9 cases of intestinal obstruction. Eleven patients were boys and 3 were girls, all of the girls suffering from obstruction. Bloody stools were present in 8 cases. There were 8 deaths, resulting in a mortality of 57 per cent. Operation is imperative when Meckel's diverticulum has been diagnosed or suspected, since perforation is a possibility with either ulceration or inflammatory changes. A careful search should be

made for Meckel's diverticulum whenever the abdomen is opened on a diagnosis of acute appendicitis and the state of the appendix does not explain adequately the symptoms or the findings of a generalized peritonitis. Everhart condemns the widespread routine medical practice of attempting closed reduction of an intussusception by means of a barium enema or by the introduction of water under high pressure because Meckel's diverticulum is so frequently associated with intussusception in infants and young children. This method of treatment is dangerous because it might only appear to be successful—though later autopsy might prove its failure—and because rupture of the friable walls of the diverticulum or of the bowel might occur.

RAUH, Cincinnati.

FOREIGN BODIES SWALLOWED BY CHILDREN. C. JOSEPH DELANEY, New York State J. Med. **40**:1024 (July 1) 1940.

Forty-one cases in which foreign bodies were swallowed and which were observed in the children's surgical service at Bellevue Hospital for the past ten years are reported. Most of the patients were under 3 years of age. All sorts of articles were swallowed, including open safety pins, straight pins, nails, screws, etc. No objects pointed at both ends, such as needles and toothpicks, were seen. In no case was an operation necessary. The children were studied by roentgenographic and fluoroscopic examinations. The average time observed for all cases was four and one-half days. One child required thirty days to pass two "bobby pins." No cathartics were given. The stools were watched carefully. Delaney expresses the belief that a regular diet brings about the same results as are obtained with special diets. He criticizes operation in cases of this kind before due time has been given for natural passage of the article. "Practically all objects will pass if one is patient enough." One case is cited of a boy who swallowed objects to win bets. He was operated on ten times. Parents of patients should be warned against giving emetics, because vomiting may lodge the object in the esophagus.

AIKMAN, Rochester, N. Y.

CALCIUM IN ACUTE PANCREATIC NECROSIS. HUGH A. EDMONDSON and IRVING A. FIELDS, Proc. Soc. Exper. Biol. & Med. **45**:803 (Dec.) 1940.

The calcium content of the pancreas and of the peripancreatic tissue was found to be increased in the presence of acute pancreatic necrosis. On calculation the excess calcium in these tissues was equivalent to the total amount of calcium in the blood and extracellular fluid. Subsequent studies showed that a moderate decrease in the serum calcium occurred on the third to eleventh day of illness in 11 patients suffering from clinical acute pancreatic necrosis. The splitting of fat by lipase with the formation of calcium soaps probably caused the tetany observed in 1 case of acute pancreatic necrosis.

HANSEN, Minneapolis.

OBSERVATIONS ON MEGACOLON (HIRSCHSPRUNG'S DISEASE), WITH SPECIAL REFERENCE TO AN ASSOCIATION WITH CHANGES IN THE FUNDUS OCULI AND HYDROCEPHALUS. C. WORSTER-DROUGHT and J. SHAFAR, Brit. J. Child. Dis. **37**:153 (July-Sept.) 1940.

The authors cite 3 instances of megacolon associated with changes in the fundus.

They report a case of congenital megacolon and congenital hydrocephalus coexisting in a boy 8 years of age. Atrophy of the optic nerve was demonstrated. They state that the hypothalamus occupies an important place in the preservation of the balance between the sympathetic and the parasympathetic nervous system. They believe it conceivable that an embryologic defect attributable to hydrocephalic expansion of the third ventricle might cause a derangement of intestinal motility and so result in megacolon.

LANGMANN, New York.

VINCENT'S DISEASE TREATED WITH NICOTINIC ACID. J. D. KING, Lancet **2**:32 (July 13) 1940.

Four patients with severe Vincent's disease were successfuly treated with nicotinic acid by mouth. Decided improvement occurred within the first twenty-four hours. The possible asociation of pellagra and Vincent's disease is discussed. It is suggested that Vincent's disease may also be related to deficient intake or utilization of nicotinic acid and its allied pyridine derivatives of the vitamin G (B_2) complex.

LANGMANN, New York.

CHRONIC JEJUNO-ILEAL INSUFFICIENCY: PATHOGENESIS OF CELIAC DISEASE, TROPICAL SPRUE AND OTHER CONDITIONS. T. IZOD BENNETT and C. HARDWICK, Lancet **2**:381 (Sept. 28) 1940.

A clinical syndrome is now more or less generally recognized consisting of fatty diarrhea, macrocytic anemia, tetany and other manifestations of hypocalcemia and of deficiencies of various vitamins. Celiac disease and tropical sprue, diseases in no way related to one another, are the commonest causes of this syndrome. It is further encountered in some cases of gastrocolic or enterocolic fistula of malignant or nonmalignant origin and in rare cases in which the intestinal lacteals are involved by fibrotic tuberculous lesions or by such processes as lymphoma or lymphosarcoma.

In every instance of this syndrome the cause of the clinical picture is the same, i. e., chronic jejunoileal insufficiency, with consequent defects of secretion and absorption. The final proof of this is provided by cases in which the small intestine is deprived of its functions by surgical short circuiting.

LANGMANN, New York.

TROUBLES OF MOTILITY AND GASTRIC SECRETION IN CHILDREN. SÉBASTIAN PINELES, Bull. Soc. de pédiat. de Iasi **10**:54, 1939.

Five cases are discussed in which roentgen ray study showed delayed emptying of the stomach and hypersecretion of gastric mucus. The patients (children) were poor eaters, complained of nausea and vague abdominal pains and were rather poorly nourished. The parents were usually nervous and the children spoiled. In 1 case a regular regimen with proper alimentation brought about disappearance of the symptoms. In the other cases cooperation was poor and there was no significant improvement.

LESLIE, Evanston, Ill.

CONGENITAL MALFORMATION OF THE BILE DUCTS. FRITZ KARLSTRÖM, Nord. med. **1**:611 (March 4) 1939.

The author reports the cases of 2 boys with atresia of the common bile ducts. One of them died at 4 months and the other at 2 months of age.

WALLGREN, Göteborg, Sweden.

A CASE OF TRICHOBEZOAR IN THE STOMACH. J. HINDMARSH, Nord. med. **1**:633 (March 4) 1939.

A mentally deficient girl of 10 years fell ill with severe abdominal pains. On examination next day a rounded, elongated, painless tumor was felt in the epigastrium. This was regarded as a scybalum. An enema did not change the picture, and a foreign body in the stomach was therefore diagnosed. At the operation a large trichobezoar filling the stomach was extracted. The girl recovered. She was a geophagist and was accustomed to swallow her hair.

WALLGREN, Göteborg, Sweden.

APPENDICITIS AND METEOROLOGY. B. KÖHLER, Nord. med. **1**:635 (March 4) 1939.

No relation was found between the incidence of acute appendicitis in children in Stockholm and the occurrence of meteorologic changes.

WALLGREN, Göteborg, Sweden.

A CASE OF CHOLELITHIASIS. M. LINDSTEN, Nord. med. **2**:1224 (April 22) 1939.

The illness in an 11 year old girl began with an attack of pain in the upper part of the abdomen and jaundice. She was then free from symptoms for three months. Later she had several attacks of abdominal pain without jaundice, appearing at irregular intervals. On examination one year after the beginning of the disease a rounded, somewhat painful swelling was found at the site of the gallbladder. Cholecystographic study showed numerous gallstones. Cholecystectomy was performed, and the girl was discharged healthy.

WALLGREN, Göteborg, Sweden.

CONGENITAL DIAPHRAGMATIC HERNIA. J. WICKSTRÖM and F. LANGENSKIÖLD, Nord. med. **2**:1418 (May 13) 1939.

A newborn full term infant had a diaphragmatic hernia on the left side with a large defect of the diaphragm. The aperture was successfully closed, and the baby was discharged healthy.

WALLGREN, Göteborg, Sweden.

A CASE OF CLINICALLY SYMPTOM-FREE CONGENITAL PYLORIC STENOSIS. NILS MALMBERG, Nord. med. **4**:3553 (Dec. 2) 1939.

A boy aged 10 months, who previously had displayed no morbid symptoms and no vomiting, fell ill with an acute catarrhal infection. On clinical examination of the abdomen peristaltic waves were seen in the region of the stomach. Roentgenographic examination showed stenosis of the pyloric part of the stomach, characteristic of congenital pyloric stenosis. Another roentgen examination, three and one-half months later, revealed the same signs, and there had still been no vomiting.

WALLGREN, Göteborg, Sweden.

ACIDOSIS IN ACUTE GASTROENTERITIS IN CHILDREN. ESBEN KIRK, Ugesk. f. læger **101**:1291 (Nov. 2) 1939.

The bicarbonate content of the blood serum of 26 children suffering from acute gastroenteritis was determined. There was no constant ratio between the decrease of the alkali reserve and the severity of the disease. In cases of healing gastroenteritis with decreased bicarbonate content of the blood serum in the beginning of the illness an increase occurred within a few days, leading to normal values for alkali reserve.

WALLGREN, Göteborg, Sweden.

Nervous Diseases

CEREBRAL DYSRHYTHMIAS IN RELATIVES OF EPILEPTIC PERSONS. LEON J. ROBINSON, Arch. Neurol. & Psychiat. **44**:1109 (Nov.) 1940.

"Electroencephalograms were obtained from 15 epileptic patients and 36 non-epileptic relatives.

"The relatives comprised 20 parents, 15 siblings and a maternal aunt. Of 15 epileptic patients, 12 (80 per cent) had abnormal electroencephalograms and 1 a doubtful tracing.

"Of the 36 relatives, 13 (36 per cent) had abnormal electroencephalograms and 10 (27 per cent) questionable.

"Judged by broad criteria for normality, cerebral dysrhythmia occurred in from one third to one half of this small group of nonepileptic persons."

BEVERLY, Chicago.

INHERITANCE OF CEREBRAL DYSRHYTHMIA AND EPILEPSY. W. G. LENNOX, E. L. GIBBS and F. A. GIBBS, Arch. Neurol. & Psychiat. **44**:1155 (Dec.) 1940.

Sixty per cent of the relatives of patients with clinical epilepsy and 10 per cent of a control group who had no near relatives with epilepsy were found to have electroencephalographic tracings typical for the disease. In only 5 per cent of the cases of epilepsy were the parents found to have normal tracings. The authors express the opinion that this is definite evidence that the dysrhythmia of epilepsy is inheritable and that such a dysrhythmia may represent a predisposition to epilepsy or some allied disorder.

BEVERLY, Chicago.

NEUROLOGIC SIGNIFICANCE OF PLATYBASIA. W. A. GUSTAFSON and ERIC OLDBERG, Arch. Neurol. & Psychiat. **44**:1184 (Dec.) 1940.

Platybasia is a deformity of the base of the skull. The foramen is pushed up into the posterior fossa; it is usually small and misshapen, and the atlas usually becomes occipitalized. The condition may produce pressure symptoms of hydrocephalus in a child or symptoms of syringomyelia in an adult. Five cases are reported.

The relation of this syndrome to the Klippel-Feil syndrome has been suggested. This condition is also differentiated from the Arnold-Chiari malformation, in which there is an elongation of the pons and medulla with herniation of the cerebellum into the spinal canal.

BEVERLY, Chicago.

JUVENILE FAMILIAL AMAUROTIC IDIOCY (VOGT-SPIELMEYER DISEASE): REVIEW OF LITERATURE AND CLINICAL REPORT OF A CASE. SOL LEVY and OLGA A. G. LITTLE, Arch. Neurol. & Psychiat. **44**:1274 (Dec.) 1940.

The authors report a case of familial amaurotic idiocy, juvenile type, emphasizing the clinical, psychologic and electroencephalographic aspects of the disease. There is also a review of the literature.

BEVERLY, Chicago.

PETECHIAL HEMORRHAGES OF THE BRAIN EXPERIMENTALLY PRODUCED IN RATS BY CONCUSSION. WALTER F. SCHALLER, K. TAMAKI and HENRY W. NEWMAN, Arch. Neurol. & Psychiat. **45**:1 (Jan.) 1941.

The authors found petechial hemorrhages in the brains of rats after trauma to the head which were comparable to those found in human brains after deaths following injury. The vascular changes were petechiae due to diapedesis, thrombotic and hyaline vascular changes and hemolysis. The changes were proportional to the severity of the trauma.

The pathologic lesions were different from those of contusion, laceration and tearing; they were the result of vascular dilatation, statis and anoxemia.

BEVERLY, Chicago.

MECHANISM OF DISPLACEMENT OF THE VENTRICULAR SYSTEM IN CHILDREN WITH ATROPHIC LESIONS. BRONSON CROTHERS and GEORGE M. WYATT, Arch. Neurol. & Psychiat. **45**:246 (Feb.) 1941.

This excellent article, which includes good reproductions of encephalograms, points out the reasons for the lateral movement of midline structures to the contralateral ventricle in cases in which unilateral atrophy predominates. The authors have demonstrated that the shift of the midline structures is due to the growth of

the more normal cerebral hemisphere, which pushes the structures to the opposite side, rather than to traction from adhesions. This explains the reason for the maximum dislocation of the median structures when the changes in the brain occur early in life.

BEVERLY, Chicago.

AN AMERICAN FAMILY WITH PELIZAEUS-MERZBACHER DISEASE. CARL D. CAMP and K. LÖWENBERG, Arch. Neurol. & Psychiat. **45**:261 (Feb.) 1941.

Pelizaeus-Merzbacher disease is one of the progressive, deteriorating diseases of the central nervous system. This condition is characterized pathologically by a diffuse sclerosis in island formations. There has been some question regarding the similarity of this condition to that described by Lowenberg and Hill in 1933. In this article, the authors describe a family of which many of the members suffered from a progressive deterioration of the central nervous system, which seems to indicate that the two conditions belong in the same group.

BEVERLY, Chicago.

AN ADAPTATION OF THE SAYRE APPARATUS FOR USE IN ENCEPHALOGRAPHY. ESTHER H. READ, Arch. Neurol. & Psychiat. **45**:319 (Feb.) 1941.

The author describes an improved Sayre apparatus for use in encephalography.

BEVERLY, Chicago.

CONGENITAL ABSENCE OF THE CRANIAL VENOUS SINUSES ON THE RIGHT. HENRY L. WILLIAMS and O. E. HALLBERG, Arch. Otolaryng. **33**:78 (Jan.) 1941.

Anomalies of the cranial venous sinuses found at operation, as reported in the literature, are discussed. The illustrative case of an 11 month old boy, is presented. In an effort to expose the sigmoid sinus a huge epidural abscess was opened. Preoperative findings typical of sepsis from involvement of the sigmoid sinus failed to reveal the manner in which a hemolytic streptococcus entered the blood stream. The operative and therapeutic measures employed are detailed.

GREENWOOD, Chicago.

INFLUENZAL MENINGITIS. RUTH ALEMAN, New Orleans M. & S. J. **93**:25 (July) 1940.

The author gives a comprehensive review of the literature and an excellent bibliography. She reports 2 cases of her own, in each of which there was a fatal outcome. In each case sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) was used in conjunction with other forms of treatment.

Statistically, sulfapyridine and sulfanilamide seem to have been beneficial in other cases cited by the author. Sound conclusions cannot yet be drawn regarding their use, but the collected evidence leads one to have hope for the future.

BERKLEY, Los Angeles.

OTOGENOUS PARIETAL CEREBRAL ABSCESS DUE TO PNEUMOCOCCUS TYPE III: RECOVERY AFTER DRAINAGE, SPECIFIC ANTISERUM, AND SULFANILAMIDE; REPORT OF A CASE. WALLACE B. HAMBY, DEWITT H. SHERMAN, CLAYTON W. GREENE and ERNEST WITEBSKY, New York State J. Med. **40**:627 (April 15) 1940.

A right parietal abscess, probably originating in subclinical otitis media of the right ear (there had been frank otitis media on the opposite side), is described in an 8 year old girl. The abscess, which was due to pneumococcus type III, was excised. The child later had cerebral hernia. Sulfanilamide and pneumococcus type III rabbit serum were administered. The child recovered but still shows residual symptoms.

AIKMAN, Rochester, N. Y.

PNEUMOCOCCUS MENINGITIS WITH HEMATEMESIS IN AN INFANT OF EIGHT MONTHS. P. LETONDAL, Union méd. du Canada **69**:811 (Aug.) 1940.

An infant of 8 months presented the typical picture of meningitis. Pneumococci were found in the cerebrospinal fluid. The baby began to vomit dark blood (at this age vomited blood is never red), and death occurred on the third day. Sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) was given, to no avail. At autopsy generalized purulent meningitis was found, with no lesions in the ears, mastoids or lungs. The stomach was normal, but there was a small superficial ulcer of the first portion of the duodenum. DAFFINEE, Boston.

CONGENITAL SPASTIC HEMIPLEGIA IN ONE OF UNIOVULAR TWINS. T. BRANDER, Nord. med. **2**:1079 (April 15) 1939.

The author reports on 3½ year old twin boys of a family with no other known case of neuropsychiatric disease. The first-born twin was healthy after a normal delivery; the other boy was extracted in primary breech presentation. The twins were full term infants with birth weights of 3,400 and 3,450 Gm. Shortly after birth the second child displayed signs of an intracranial lesion, and when seen at 3½ years of age he showed slight spastic hemiplegia of the left side. The author emphasizes the importance of detailed records of the parturition in studies on twins, especially when there is a question of studying the heredity of neuropsychiatric diseases. WALLGREN, Göteborg, Sweden.

DIFFUSE CEREBRAL SCLEROSIS (KRABBE) IN CHILDREN. OLOF BRANDBERG, Nord. med. **4**:3558 (Dec. 2) 1939.

The 3 children (1 girl and 2 boys) of a farmer showed normal development until they were 2 years of age. At this time they displayed difficulty in walking, rigidity of the arms and legs, convulsions, impaired sight (atrophy of the optic disks), psychic retardation and an increased globulin content of the otherwise normal spinal fluid. The Wassermann reactions were negative. The children died at the age of about 3 years. Histologic examination in 1 case showed the typical picture of diffuse cerebral sclerosis described by Krabbe.

WALLGREN, Göteborg, Sweden.

Psychology and Psychiatry

ELECTROENCEPHALOGRAMS OF "CONSTITUTIONALLY INFERIOR" AND BEHAVIOR PROBLEM CHILDREN: COMPARISON WITH THOSE OF NORMAL CHILDREN AND ADULTS. DONALD B. LINDSLEY and KATHARINE KNOX CUTTS, Arch. Neurol. & Psychiat. **44**:1199 (Dec.) 1940.

Behavior problem children were found to have electroencephalographic tracings which differed somewhat from those of a group of children and adults not presenting behavior disorders. BEVERLY, Chicago.

PREVENTION OF DISABLING DISORDERS. P. HANSTEEN, Nord. med. **1**:725 (March 18) 1939.

Insanity, psychopathy and feeblemindedness are predominantly caused by inheritance. Epilepsy, deafness, blindness, alcoholism and criminality are in some degree due to inherited predisposition. There seems to have been no retrogression of these disorders within the last century. If such conditions are to be prevented, society must support the desirable inherited qualities and subdue the undesirable ones. Increasing birth control tends to curtail familial good qualities, but the number of defective children is increased, thanks to lack of birth control

in inferior families. A compulsory medical examination before marriage, a greater effectiveness of the sterilization law and a more frequent use of sterilization of persons suffering from the aforementioned diseases before their discharge from institutions are recommended.

WALLGREN, Göteborg, Sweden.

PSYCHOSIS IN CHILDHOOD. K. OTTO AF KLERCKER, Nord. med. **2**:1223 (April 22) 1939.

Attention is drawn to the rare incidence of true psychosis in childhood and to the unsatisfactory knowledge and lack of personal experience of the pediatrician and the psychiatrist. Cooperation of these two specialties is recommended in order to facilitate accumulation of experience and knowledge and to insure proper care and treatment of children with this condition.

WALLGREN, Göteborg, Sweden.

Diseases of the Genitourinary Tract

THE BEHAVIOR OF RENAL BLOOD FLOW AFTER PARTIAL CONSTRICTION OF THE RENAL ARTERY. HENRY A. SCHROEDER and J. MURRAY STEELE, J. Exper. Med. **72**:707 (Dec.) 1940.

Experimental evidence is presented to show that renal blood flow is not appreciably altered by changes in blood pressure, partial constriction of the renal artery or systemic injection of vasoconstricting or vasodilating drugs. This is presented as favoring the concept of control of renal circulation independent of systemic blood pressure.

BILLINGTON, Seattle.

A PEDIATRIC-UROLOGIC PROBLEM: CONGENITAL VALVES OF THE POSTERIOR URETHRA WITH CASE REPORT. WALTER M. KEARNS and EDWARD B. JACOBSON, Wisconsin M. J. **39**:603 (Aug.) 1940.

The incidence of anomalies in the urogenital tract is greater than in any other system in the human body, being present in about 2.3 per cent of children who come to autopsy. Valves of the posterior urethra, next to stenosis of the urinary meatus, are the most common cause of congenital infravesical obstructions and are of extreme clinical importance because of producing urinary back pressure. Unrecognized, this anomaly may cause even fatal changes in the upper portion of the urinary tract.

The symptoms are: disturbances in urination, ranging from frequency and dysuria to complete retention, renal impairment and evidences of infection. Sometimes only gastrointestinal symptoms are evident. Cystoscopic and urethroscopic diagnosis will confirm the diagnosis, and transurethral removal of the valves is the treatment of choice.

Prognosis depends on the amount of destruction that has occurred in the upper portion of the urinary tract. This destruction may begin in utero, since the fetal kidney begins to function at about the fifth month of intrauterine life.

A case report of a premature male infant with nearly complete obstruction is given. An operation was performed, but the child died on the sixteenth day from pyelonephritis and uremia.

JANNEY, Wauwatosa, Wis.

GIANT URINARY BLADDER IN A NEWBORN INFANT. KAARE BENDIXEN, Nord. med. (Med. rev., Bergen) **2**:1771 (June 10) 1939.

The author reports the postmortem observations on a newborn infant. Great distention of the urinary bladder was found, without any demonstrable obstruction of the urethra. The kidneys were atrophic.

WALLGREN, Göteborg, Sweden.

TRANSITORY DIABETES INSIPIDUS. JUSTUS STRÖM, Nord. med. **4**:3554 (Dec. 2) 1939.

In a boy 7 years of age apparently primary diabetes insipidus developed spontaneously. Examination of the specific gravity and of the sodium chloride concentration of the urine disclosed an impaired concentration capacity of the kidneys. Six weeks later all symptoms had vanished and the renal concentration capacity was normal. The author expresses the belief that the diabetes insipidus in this case was due to a toxic lesion of the neurovegetative organs produced by an acute infection.

WALLGREN, Göteborg, Sweden.

VITAMIN P IN HEMORRHAGIC NEPHRITIS. T. GRINSING, Ugesk. f. læger **101**: 117 (Jan. 26) 1939.

Seven children with acute hemorrhagic nephritis were treated with repeated intravenous injections of vitamin P, without success.

WALLGREN, Göteborg, Sweden.

Diseases of the Ductless Glands; Endocrinology

INDUCTION AND COURSE OF PERMANENT DIABETES PRODUCED BY ANTERIOR PITUITARY EXTRACT. F. C. DOHAN, C. A. FISH and F. D. W. LUKENS, Endocrinology **28**:341 (March) 1941.

Ten dogs were made permanently diabetic by means of intraperitoneal injections of anterior pituitary extract.

Many observations as to the course and nature of the disease are recorded. It was found that the use of large doses of protamine zinc insulin daily during the injection of anterior pituitary extract prevents the development of diabetes, of hydropic degeneration of the islands and of the reduction in the insulin content of the pancreas which follow pituitary treatment without insulin. Manifestations of the thyrotropic and gonadotropic, as well as of the glycotropic (contrainsulin), effects of pituitary extract observed during the period of injection were absent in the permanent phase of diabetes, suggesting that overactivity of the pituitary was not responsible for the persistent diabetes.

JACOBSEN, Buffalo.

THE HEPATIC GLYCOGEN RESERVES IN DIABETES MELLITUS. I. ARTHUR MIRSKY, MORTON KORENBERG, NORTON NELSON and WALDO E. NELSON, Endocrinology **28**:358 (March) 1941.

As the administration of phlorhizin has been shown to have no permanent harmful effects, the authors have used it to determine the severity of diabetes in man. By the administration of phlorhizin glycosuria is produced, resulting in the removal of circulating sugar, and only a large glycogen reserve in the liver will insure a relatively constant blood sugar. In cases in which the glycogen reserve is inadequate the blood sugar level drops and ketosis may develop. This offers a means of determining the extent of the glycogen reserve, which is in inverse proportion to the severity of the diabetes.

In the course of the investigation it was noted that children cannot retain carbohydrate to the same degree as do adults because of an apparent increased rate of glycogenolysis. This fact is true not only for diabetic children but also for normal children and accounts for their greater susceptibility to ketosis and coma.

JACOBSEN, Buffalo.

CLINICAL TRIALS WITH INSULIN-QUININE MIXTURES BY MOUTH IN DIABETICS. WINDSOR C. CUTTING and G. BERNARD ROBSON, Endocrinology **28**:375 (March) 1941.

After having studied mixtures of insulin and a variety of pharmacodynamic agents of known general properties and effects for absorption in ligated intestinal

loops and by rectum in rabbits, on gastric administration in mice and rats and on oral and rectal administration in man, the authors found that the oral administration of quinine with insulin to normal persons resulted in definite, though fleeting, hypoglycemia, thus confirming the results of experiments in animals. Insulin-quinine mixture was then administered to 10 diabetic patients, with encouraging results, although about one-half the patients showed the well known side actions of cinchonism in variable degrees.

JACOBSEN, Buffalo.

INHIBITION AND STIMULATION OF TESTES IN RATS TREATED WITH TESTOSTERONE PROPIONATE. HARRY SHAY, J. GERSHON-COHEN, KARL E. PASCHKIS and SAMUEL S. FELS, Endocrinology **28**:485 (March) 1941.

Experiments on rats are reported which are interpreted as follows:

"Testosterone propionate is thought to stimulate the testes directly, at the same time exerting an inhibitory influence on the pituitary. This in turn inhibits the testes through inhibition of the gonadotropic pituitary hormone. During the first month of life the stimulating effect is not counteracted by inhibition of the pituitary, because gonadotropic function is not yet developed."

JACOBSEN, Buffalo.

THE EFFECT OF TESTOSTERONE PROPIONATE ON THE RAT TESTIS. H. S. RUBINSTEIN and A. A. KURLAND, Endocrinology **28**:495 (March) 1941.

Experiments on rats are reported which are interpreted as follows:

"Testosterone propionate in small dosage stimulates proliferation of the germinal epithelium. Upon increasing the dose testosterone propionate depresses the pituitary gland which in turn inhibits testicular growth and spermatogenesis so that with markedly excessive doses, degeneration follows. As the dosage is still further increased the gigantic proportions of the reacting secondary sex organs become so striking that much of the injected hormone is utilized merely for their maintenance. This diminishes blood androgen concentration thereby depressing to a lesser degree the anterior lobe of the pituitary. The testis is thus correspondingly spared."

JACOBSEN, Buffalo.

THE NEW YORK DIABETIC ASSOCIATION: SUMMER CAMP FOR UNDERPRIVILEGED DIABETIC CHILDREN. FREDERICK W. WILLIAMS and JAMES FINLAY HART, New York State J. Med. **40**:795 (May 15) 1940.

The association conducts a summer camp for underprivileged diabetic children, supported entirely by voluntary contributions. In all, 155 vacations were given to 106 diabetic children. The object is to provide a fresh air excursion lasting two weeks for children who are excluded from other camps because of diabetes. The children were instructed in making examinations of the urine, in giving injections of insulin and in estimation of diet. It has been shown that there is a definite need in the city of New York for such a camp.

AIKMAN, Rochester, N. Y.

VITAMINS D_2 [CALCIFEROL] AND D_3 AND A.T. 10 [DIHYDROTACHYSTEROL] IN CONGENITAL THYROID AND PARATHYROID DEFICIENCY. H. P. HIMSWORTH and MONTAGUE MAIZELS, Lancet **1**:959 (May 25) 1940.

The authors describe a case of congenital thyroid and parathyroid deficiency associated with tetany and epilepsy in a boy aged 13. When first seen the boy had a basal metabolic rate of —25 per cent; the value for serum calcium was 5 mg. and that for inorganic phosphate 9 mg. per hundred cubic centimeters.

Successful treatment of the tetany had no effect on the symptoms of thyroid deficiency, nor did treatment of the thyroid deficiency alone influence the development of tetany.

When the value for blood calcium rose above 7 mg. per hundred cubic centimeters the epileptic fits and tetany disappeared.

The parathyroid deficiency was controlled by the oral administration of vitamin D_2 (calciferol) in oil, 500,000 international units weekly.

Dihydrotachysterol (A.T. 10) was less reliable in its action than vitamin D_2 (calciferol). Vitamin D_3 was equivalent to vitamin D_2 in controlling the parathyroid deficiency.

LANGMANN, New York.

STUDIES ON MECHANISM OF INSULIN CONVULSIONS: I. SIGNIFICANCE OF SERUM ELECTROLYTES. II. EFFECTS OF BREATHING ATMOSPHERES VARYING WIDELY IN OXYGEN AND CARBON DIOXIDE CONTENT. IRVINE MCQUARRIE, M. R. ZIEGLER and W. E. STONE, Chinese M. J. **58**:1 (July) 1940.

The authors wished to learn from these experiments whether light might be thrown on the subject of idiopathic epilepsy and its functional disturbances in childhood. Studies were made on dogs by various procedures affecting the electrolytes of the serum and the occurrence of insulin convulsions. They found that convulsive reactivity was definitely diminished by a reduction of the oxygen or an increase in the carbon dioxide tension of the atmosphere. In the absence of insulin, the breathing of a gas compound of 88 to 95 per cent nitrogen and 12 to 5 per cent oxygen produced in the serum a lowering of the potassium and inorganic phosphorus as well as of the carbon dioxide tension, but it did not make any other change in the electrolytes.

The elevation of the atmosphere by 10 to 15 per cent of carbon dioxide caused little effect on the potassium but a definite rise in inorganic phosphorus and carbon dioxide tension of the plasma. When either oxygen or carbon dioxide was added to the atmosphere hyperglycemia was caused. NEFF, Kansas City, Mo.

STUDIES ON MECHANISM OF INSULIN CONVULSIONS: EFFECTS OF VARYING PARTIAL PRESSURES OF ATMOSPHERIC OXYGEN AND CARBON DIOXIDE IN ADRENALECTOMIZED ANIMALS. I. MCQUARRIE, M. R. ZIEGLER, W. E. WANGENSTEEN and C. DENNIS, Chinese M. J. **58**:26 (July) 1940.

The studies on the mechanism of insulin convulsion are continued in adrenalectomized dogs.

NEFF, Kansas City, Mo.

Diseases of the Muscles, Bones, Joints and Lymph Glands

DYSCHONDROPLASIA (OLLIER) OF THE UPPER LIMB WITH OTHER DEVELOPMENTAL ABNORMALITIES. T. ANWYL-DAVIES and F. PARKES WEBER, Brit. J. Child. Dis. **37**:110 (April-June) 1940.

Dyschondroplasia (Ollier) is a developmental abnormality of dysplastic origin affecting the growing ends of long bones, including the smaller long bones of the hands and feet.

An instance of this disease in a girl of 10½ years is reported. The right upper extremity showed deformities, consisting of thickened, distorted and nodular thumb, index finger and middle finger and swelling of the lower end of the radius and of the upper end of the humerus, which was shortened and bent outward. There were also mental deficiency, bilateral epicanthus, "fleshy" upper eyelids and eroded teeth. The family history was irrelevant as far as congenital deformities or developmental dysplasia were concerned.

LANGMANN, New York.

A Case of Multiple, Probably Hereditary, Epiphysial Anomalies of the Skeleton. S. Siwe, Nord. med. **2**:1225 (April 22) 1939.

The patient was a boy aged 11 years. At 3 years of age he had been treated at the pediatric clinic of Lund for chronic polyarthritis; he had been discharged improved and was able to attend school from 7 to 11 years of age. Then he suffered from pains in his knees. Roentgenographic examination displayed normal joints, but there was a systemic disorder of the epiphysial cartilages. An 8 year old brother showed the same changes but presented no symptoms.

Wallgren, Göteborg, Sweden.

Bilateral Epiphysiolysis Capitis Femoris Treated by the Method of Smith-Petersen. J. Spotoft, Nord. med. (Hospitalstid.) **2**:1736 (June 10) 1939.

This disease in a girl of 14 was successfully treated by bloodless reposition and osteosynthesis by the method of Smith-Petersen. The previously used methods of treatment are discussed, and the advantage of the present one is emphasized.

Wallgren, Göteborg, Sweden.

Boeck-Besnier-Schaumann Disease in a 10 Year Old Boy. A. Biering, Nord. med. (Hospitalstid.) **4**:3361 (Nov. 18) 1939.

The chief signs in this case were fever of long duration, generalized peripheral glandular enlargement and slight involvement of the pulmonary hili. There were no cutaneous lesions. The diagnosis was confirmed by biopsy of a swollen lymphatic gland. The condition was unchanged during three months of observation.

Wallgren, Göteborg, Sweden.

Skin Diseases; Allergy

The Failure of Histaminase to Protect Guinea-Pigs Against Histamine and Anaphylactic Shock. H. L. Alexander and Donald Bottom, J. Immunol. **39**:457 (Dec.) 1940.

The authors were unable to demonstrate any protection from histamine or anaphylactic shock in guinea pigs by the use of histaminase. This was contrary to work of other investigators.

Billington, Seattle.

Influence of Electrolytes on the Cutaneous Reactivity of Seitz-Filtered Ragweed Solutions. C. A. Kock, A. R. Zoss and R. S. Hirose, J. Immunol. **39**:461 (Dec.) 1940.

Solutions of ragweed antigen which were free of electrolyte still produced intracutaneous reactions in ragweed-sensitive subjects. If the same electrolyte-free solutions were passed through an electrolyte-free Seitz filter, the filtrate produced no reaction in ragweed-sensitive subjects. The filtrate could be reactivated by adding electrolyte as salt solution. The cause of this alteration could not be determined.

Billington, Seattle.

Follicular Hyperkeratosis: A Sign of Malnutrition? John Pemberton, Lancet **1**:871 (May 11) 1940.

Examination of 3,000 children and adolescents in various centers in Great Britain during a nutritional survey revealed follicular hyperkeratosis in 5 per cent. The eruption consisted of crops of enlarged hair follicles appearing first on the extensor aspects of the arms, legs and buttocks and later and less commonly over

the scapulas, back and abdomen. Histologically there were keratosis of the skin surrounding the hair follicles, absence of the sebaceous glands and atrophy of the sweat glands, together with distention or plugging of the hair follicles with keratotic debris.

The condition is probably an early sign of a deficiency of vitamin A or of fat.

LANGMANN, New York.

Surgery and Orthopedics

TO AVOID CIRCUMCISION. CHEVALLEY, Nourrisson **28**:68 (March) 1940.

A paper by Lavergne (*Nourrisson* **27**:280 [Sept.] 1939) is referred to in which a routine procedure is described by which circumcision need not be performed even on patients with phimosis. The use of a Terrier forceps instead of a probe is suggested by Chevalley in order to loosen the adhesions. The forceps is introduced into the orifice of the prepuce and only thereafter opened slowly. The prepuce is thus sufficiently dilated to permit manual reduction of the phimosis. This procedure can be repeated frequently. The use of petrolatum between treatments is recommended to keep the skin and the adhesions soft.

HEYMANN, Cleveland.

SKULL FRACTURE IN INFANTS. H. DIERKER, Kinderärztl. Praxis **11**:73 (March) 1940.

Dierker saw 4 infants with fracture of the skull within two years. In each case there were no symptoms other than the history of a fall and the external hematoma. Roentgenograms of the skull were therefore taken. The administration of phenobarbital was the only treatment that seemed necessary. The prognosis in cases of this kind is good. The taking of routine roentgenograms of the skull is advocated as the only means of avoiding failure in diagnosis of fracture of the skull.

HEYMANN, Cleveland.

Teeth and Dentistry

A SURVEY OF NUTRITION AND DENTAL CARIES IN 120 LONDON ELEMENTARY SCHOOL CHILDREN. IRENE ALLEN, Brit. M. J. **1**:44 (Jan. 11) 1941.

This apparently was a fact-finding study, in which no definite conclusions were reached.

ROYSTER, University, Va.

TREATMENT OF DENTAL CARIES. M. DECHAUME, Presse méd. **48**:1057 (Dec. 18-21) 1940.

Dechaume stresses the thesis that caries is due to local and trophic disturbances rather than to general deficiencies. In the treatment of the inflammatory lesions of the tooth a nonirritating antiseptic can be utilized. Excision of the dentine down to the pulp will produce devitalization of the tooth in many cases.

DAFFINEE, Boston.

ALIMENTARY AND MEDICINAL PROPHYLAXIS AND THERAPY OF DENTAL CARIES. O. BRINCH, Nord. med. **1**:83 (Jan. 14) 1939.

It is not possible to improve resistance against dental caries by diet or by pharmacologic compounds when the teeth are already developed, as there is no vital metabolism in the enamel of the teeth. The dietetic prophylaxis of dental caries is confined to the period during which the teeth are growing. It is impor-

tant that the diet during this period contain a sufficient supply of calcium, phosphorus and vitamins and that the food be of such a consistency that it necessitates chewing.

WALLGREN, Göteborg, Sweden.

RELATION BETWEEN VITAMIN C AND DENTAL CARIES. T. SANDBERG and H. DAGULF, Nord. med. (Hygiea) **1**:603 (March 4) 1939.

One hundred and ninety healthy school children and children hospitalized for surgical treatment of different kinds of tuberculosis were studied. Determination of the ascorbic acid level of the blood (Farmer and Abt) was carried out in the spring and in the fall. In some cases saturation tests were performed. The teeth were carefully examined by a dental surgeon before and after the study. There was no statistically significant difference in the degree of dental caries in children with satisfactory and in children with abnormal vitamin C standards.

WALLGREN, Göteborg, Sweden.

Miscellaneous

PRACTICAL PROBLEMS OF A PHYSICIAN WITH A COMBINED OBSTETRIC AND PEDIATRIC PRACTICE. H. A. SINCOCK, Wisconsin M. J. **39**:827 (Oct.) 1940.

The author states the belief that the "obstetrico-pediatrician" has a distinct advantage in caring for children since he can consider preventive care for them during the prenatal period and during delivery, at which times too little consideration is usually given them. Being pediatrically minded he will also spend more time preparing the mother physically and mentally for successful nursing and care of the infant, the prevention of difficulties always being paramount. Methods for promoting breast feeding are described.

In 150 cases taken at random from his file Dr. Sincock found no correlation between the gain in weight of the mother during pregnancy and the weight of the infant.

The author has done his last 400 circumcisions at the time of the birth. This permits healing before the infant leaves the hospital, and there is less tendency toward bleeding.

JANNEY, Wauwatosa, Wis.

REPORT OF THE JUVENILE COURT. LUIS ANTONIO MORZONE, Bol. Inst. internac. am. de protec. a la infancia **14**:247 (Oct.) 1940.

The author, a judge of the juvenile court, gives an account of the work done in the juvenile court of La Plata during the first year of sitting, emphasizing the difficulties encountered. The report draws attention to the importance of certain details given by the social workers, showing by their information that the social factors are almost always of essential value in the study of infantile delinquency. The mission of the physician is also of the greatest importance in the work of the court; the diagnosis arrived at by him facilitates the accurate solution of the problem presented to the court.

FROM EDITOR'S SUMMARY.

CURRENT EDUCATIONAL ISSUES AND THEORIES. EMILIO FOURNIÉ, Bol. Inst. internac. am. de protec. a la infancia **14**:265 (Oct.) 1940.

It is recommended that the American schools favor the liberty of the child, respecting his personality, so as to attain an ample balance between liberty and subordination. For this it is necessary that the teacher base his authority not on violence or on extreme strictness but on science, experience, culture and honesty; on the other hand, the child should find in his home the same understanding of his necessities and should observe there examples of all virtues. From the prac-

tical point of view, the nation and the authorities should give to education (primary, secondary and vocational), in a permanent and decided way, all the necessary support so that its benefits may reach children and youths of every age and without exception, regardless of social status. FROM EDITOR'S SUMMARY.

INFANT OF 1½ YEARS KILLED BY ELECTRIC CURRENT WHILE PLAYING WITH AN ELECTRIC LAMP. E. HVAL and K. BENDIXEN, Nord. med. (Med. rev., Bergen) **1**:913 (March 31) 1939.

The child was found dead with both hands clasped around an electric lamp. The lamp was supplied with a metal shade stand. This was readily displaced in such a manner that contact was brought about with the electric current socket. Further, the electric wire was faulty and revealed several broken threads. Only by manipulating the wire could contact be established. It is probable that the accident occurred while the boy put one hand on the displaceable metal shade stand and the other hand on the electric bulb at an instant when contact was established. The lamp carried 220 volts. Autopsy revealed characteristic electric current marks on the left index finger and on the right thumb, traumatic emphysema, edema of the brain and status thymicolymphaticus.

WALLGREN, Göteborg, Sweden.

MODEL WARD FOR CHILDREN. A. LICHTENSTEIN, C. GYLLENSWÄRD, U. NORDWALL and H. CEDERSTRÖM, Nord. med. (Hygiea) **2**:1575 (May 27) 1939.

The authors describe a model ward in a children's hospital for 22 infants and 20 older children. Special attention is called to measures to prevent the spread of infections in the ward and during visits to the outpatient department.

WALLGREN, Göteborg, Sweden.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

PHILIP ROSENBLUM, M.D., *President*

A. L. NEWCOMB, M.D., *Secretary*

Regular Meeting, March 18, 1941

The Inadequately Treated Cretin. DR. I. P. BRONSTEIN and DR. W. H. REALS.

The child with inadequately treated hypothyroidism may present diagnostic problems related to growth, and because of this a tendency has arisen to ascribe to cases in which the stature is below normal an element of deficient production of the growth-stimulating factor of the anterior lobe of the pituitary and to administer an anterior pituitary extract containing this principle, exclusively or in combination with wholly inadequate thyroid therapy. The associated pallor in such cases may lead to the diagnosis of secondary anemia of unknown cause. The constipation, protuberance of the abdomen and megacolon which may be present may be mistaken for symptoms of Hirschsprung's disease. In the case reported here, that of a boy aged 15 years, such diagnostic difficulties were encountered.

This child was recognized as a cretin at the age of 30 months, the symptoms apparently dating from infancy. It is uncertain whether he had congenital thyroid deficiency. He had been given treatment of various types prior to January 1940, at which time he was referred to us because of understature. The impression on cursory examination was that of a child with thyroid deficiency. Of interest was the fact that lumbar sympathectomy had been performed on account of a diagnosis of Hirschsprung's disease.

Thyroid was administered in adequate dosage, and within approximately eight months the boy was no longer recognizable as a cretin. He had shown no increase in the rate of growth after considerable treatment with the pituitary extract, but with an ample dosage of thyroid he made spectacular progress. Adequate dosage is determined by physical, osseous and mental growth; severe toxic symptoms are to be avoided.

It is emphasized that the child with inadequately treated thyroid deficiency may have symptoms simulating other conditions, a condition which leads to diagnostic errors. This patient's symptoms were due to thyroid deficiency and were corrected by adequate thyroid therapy. The child of understature should have the benefit of a diagnostic study to exclude hypothyroidism.

DISCUSSION

DR. I. P. BRONSTEIN: When I became interested in pediatric endocrinopathies one of the first things I studied was hypothyroidism. In perusing the literature at that time, I was interested to discover that in many cases the diagnosis was not made before the child reached the age of 2 or 3 years and in a small number of cases not before the patient was 6 years old. During the last six or eight years in an increasing number of cases the disorder has been recognized while the child was under the age of 1 year. From time to time one encounters patients whose condition has been neglected, but not such unusual situations as that of seeing 2 untreated children in one family, a man of 24 years and a boy of 13. Familial cretinism is common in Switzerland.

With earlier recognition and more adequate treatment we have seen fewer patients with cretinism, and I suppose we had a sort of complacent attitude until we saw this patient.

There are a few points on which I wish to comment; first is the question of the three symptoms which give rise to diagnostic difficulty. I also want to show slides which will further emphasize some of the known facts.

Children with hypothyroidism may present interesting problems with regard to the administration of the growth-stimulating factor of the anterior pituitary. There is clinical and experimental evidence of a relation between the anterior lobe of the pituitary and the thyroid gland. Shelton and associates (*Endocrinology* **27**:425 [Sept.] 1940) described the case of a 10 year old cretin with marked physical and mental retardation and two carpal centers. For more than a year they empirically employed daily doses of 2 cc. of an alkaline extract of the anterior lobe of the pituitary which contained 10 growth units per cubic centimeter, with no change in the patient's status. With administration of thyroid a spectacular result was achieved. Considerable amounts of thiamine hydrochloride were also given to this patient. A definite relation between vitamin deficiency and hypothyroidism is not yet established.

Pathologic fractures have been reported to occur in cretins receiving thyroid, caused by the fast growth of the bone, with osteoporosis. We have never observed such fractures, but we prescribe vitamin D in ample amounts for our patients. As I have already mentioned, thyroid has an excellent effect on growth, and I have often wished that pituitary extracts administered to pituitary dwarfs would yield similarly good results. In a recent series of reports on endocrine disturbances, Sevringhaus pointed out that thyroid, which is used in conjunction with anterior pituitary extract containing the growth-stimulating substance in cases of pituitary dwarfism, may hasten epiphysial closure.

There is evidence for the hematopoietic function of the thyroid gland both in animals and in human beings. The late Dr. Jaffé reported that chronic thyroiditis, discovered post mortem, was apparently responsible for the obscure anemia from which several adult female patients had suffered. The thyroid gland at necropsy was fibrosed and remarkably infiltrated with lymphocytes.

In regard to abdominal enlargement and distention with transient pain and constipation, in a number of cases reported in the literature the patients were considered to have Hirschsprung's disease and were so treated for varying periods, but fortunately none were subjected to surgical procedures. (Slides.)

Developmental Pattern of the Child as Reflected in the Calcification Pattern of the Teeth. Dr. M. Massler, Dr. I. Schour and Dr. H. G. Poncher.

This paper was published in full in the July issue of the American Journal of Diseases of Children, page 33.

DISCUSSION

Dr. Bengt Hamilton: I think that pediatricians often see defects in calcification related to too rapid growth, for example, in the premature child. I should like to ask whether the infancy ring may be related to the rate of growth during infancy and whether the rapid recovery after the age of 11 months may not mean that the velocity of growth rather suddenly decreases at that age.

Protection of Newborn Infants Against Gross Infection. Dr. James A. Reyniers (by invitation).

DISCUSSION

Dr. C. F. McKhann, Ann Arbor, Mich.: I have been following Dr. Reyniers' work with great interest. Some of his suggestions have found practical application in the design of incubators for premature babies, such as the Chapple incubator.

The subject of hospital infections is one which my associates and I have also been investigating. A paper on this subject was read at a meeting of the Chicago Pediatric Society three years ago (AM. J. DIS. CHILD. **55**:220 [Jan.] 1938). The problem is especially important in the field of pediatrics. One survey of an infants' hospital showed that approximately 10 to 12 per cent of the patients contracted infections while in the institution. This incidence reflects a great improvement in the conditions which existed thirty or forty years ago, but it is still disturbingly high. Within a hospital there exist several possible modes for spread of infection. Relatively unimportant is the likelihood of spread by insect vectors, and direct patient to patient contact is not common in most children's hospitals. Contact of the attendants' hands with the baby, direct transmission of droplets from personnel to patient or from patient to patient and more distant transfer by means of air-borne infection seem to be the most important vector lines.

One wonders which is more important, personnel to patient or patient to patient transmission of infective material. If a patient is enclosed in a room such as that described by Dr. Reyniers, patient to patient transmission is eliminated. If the room has individual outside ventilation, an added precaution is furnished. Such separate rooms with individual outside ventilation have been furnished in many hospitals, but as a rule there is not one but several babies in the room. I question very much whether the precaution of wearing a mask and gown will permit a person to enter such a room with safety to the patients.

Last year an opportunity was afforded in the Infants' Hospital, in Boston, to establish a controlled study of the effects of ultraviolet irradiation in the prevention of infection in an infants' ward. Ten cubicles in each of two wards were protected by ultraviolet lamps, while the other ten cubicles in the ward were not so protected. Gown technic was employed in both sections of the wards, but masks were worn only in the unirradiated sections. From previous investigations it was anticipated that the incidence of cross infections would be lower in the sections in which masks were worn, because the amounts of irradiation in use seemed too small to make much difference in cross infection rates and certainly such irradiation could not prevent personnel to patient transmission of infective material. My associates and I were surprised to discover at the end of the season that in the unirradiated wards, where masks were worn, the incidence of cross infections was 12.9 per cent, whereas in the irradiated wards it was only 1.8 per cent. In an air-conditioned ward for premature infants, which had an outside air intake, the bacterial counts were still lower than in the irradiated wards, but on a busy day, when many nurses were passing in and out of the air-conditioned ward, the bacterial counts rose to levels even higher than in the unirradiated wards.

It appeared that direct personnel to patient transmission was of less importance than we surmised. Nevertheless, it seemed that the question of masking of personnel merited consideration. Masks of both the deflecting and the filtering type have been suggested. Most masks now in use not only fail to protect the baby from direct expulsion of droplets but fail to prevent contamination of the surrounding air, and no mask now available for use will protect the wearer. It is possible to construct a filtering mask—and one is now available commercially—which is about 95 per cent effective in protecting the patient but is only about 70 per cent effective in protecting the wearer against droplet nuclei and organisms floating in the air. This question has been brought up periodically by workers interested in the care of tuberculous patients: If the physician wears a mask in a ward for patients with tuberculosis is he protected? Or should the patient wear the mask? If the patient wears the mask the physician will be protected against the direct expulsion of droplets by the patient but will not be protected against previous contamination of the air of the ward with tubercle bacilli. If the physician wears

the mask he will receive more protection, but at most it will be only to the extent of about 70 per cent against possible exposure.

Perhaps the important thing at present is not how effective ultraviolet irradiation is in the control of hospital infections or how important masking may be as a part of hospital procedure but rather that a general awareness of the magnitude of the problem is being developed among physicians and nurses who care for infants and children, so that further advances in air sanitation may come from the increasing attention focused on this menace of cross infections in infants' and children's hospitals.

Dr. L. W. Sauer, Evanston, Ill.: When the new Cradle building was constructed, one third of the thirty-six cubicled cribs were planned according to Professor Reyniers' design; six of them were in inner cubicles constructed according to the specifications on the blackboard. It is still too early to evaluate properly from a clinical point of view the relative efficiency and practicability of the three precautionary measures against air-borne cross infections; that is, whether air conditioning alone, with a 100 per cent intake of outside air, is sufficient, or whether such air conditioning needs to be supplemented with the bactericidal lamps of Wells or the inner cubicles of Reyniers. During the two year period (1937-1938) in the old building during which an excellent aseptic hand technic was used, 64 instances of cross infection of the respiratory tract occurred. During the two year period (1939-1940) in the new nursery 10 instances of cross infection of the respiratory tract occurred; 8 occurred in the control unit (100 per cent intake of outside air and aseptic hand technic), 1 in the Wells unit (air conditioning and bactericidal lamps), and 1 in the Reyniers unit (air conditioning and closed cubicles, of which 6 have an inner cubicle construction).

Dr. Iwan Rosenstern, Evanston, Ill.: The observations on prevention of air-borne cross infections made at the Cradle are limited to a certain age period (first three months of life) and to a certain group of air-borne infections (infections of the upper respiratory tract). The results cannot be applied to other age groups or to other types of air-borne infections, such as chickenpox or measles, without making special investigations.

The preliminary results at the Cradle show that open cubicles and air conditioning did not prevent the transmission of infections of the upper respiratory tract, either from nurse to infant or from infant to infant, while ultraviolet barriers and mechanical barriers used with the same setup were equally efficient in preventing the spread of infections of the upper respiraotry tract.

The next problem at the Cradle is to decide whether ultraviolet barriers, mechanical barriers or both types should be used. In answering this question the following points should be considered:

Ultraviolet light destroys germs, but as a powerful biologic agent affects the human body as well. Local effects on the skin and conjunctiva of the infants and nurses have been eliminated by adequate means, but further investigations on systemic effects should be made, especially when ultraviolet irradiation is made a permanent feature. No harmful systemic effects have been demonstrated so far.

Mechanical barriers are somewhat inconvenient for the nurses, since they require more manipulation, and they may interfere somewhat with the observation of the infants (hearing and seeing them); but they protect the infant from the disturbing noises of the ward.

Expense is another factor to be considered. The installation is more costly when mechanical barriers are used, but the running expenses are higher with ultraviolet lamps.

Dr. Maurice L. Blatt: The advances in the sanitary control of food and water have been slow but progressive. Dr. McKhann is following the same

channels in promoting air sanitation. It is very costly to expose soldiers to infections. The institution of methods based on the experience of Dr. Reyniers and Dr. McKhann will protect the health of adults gathering in public halls. Many institutions have to accommodate themselves to buildings built prior to the institution of these methods and have difficulty not in selling the idea of the effectiveness of such measures but in instituting the technic. Some of the influenza and cross infection in hospitals could have been obviated this year had such measures as those discussed here been in effect.

DR. JAMES A. REYNIERS: Obviously, consideration must be given to ventilation and a barrier which can be used under normal conditions in older rooms and buildings. It need not be highly complicated. By using the ventilation principle, I believe, many of the older buildings can be utilized to advantage; they will not be perfect, but they will at least be adequate.

PHILIP ROSENBLUM, M.D., *President*

A. L. NEWCOMB, M.D., *Secretary*

Regular Meeting, April 15, 1941

PRESENTATION OF CLINICAL CASES

Neurosis in a Child. DR. BERT I. BEVERLY.

A girl aged 11 years was brought in for examination eighteen months ago because of attacks of polypnea accompanied by marked anxiety. The spells began eighteen months before the first visit; they occurred from one to ten times per day and lasted for about three to fifteen minutes.

The patient is the third of 4 children. The personal history was negative for other illnesses but important in that she was always a very good girl and unusually solicitous of her mother. She wanted to help with the housework and preferred scrubbing the floors to playing with other children. The history indicated that she had been frightened since infancy and that she felt (consciously or unconsciously) that she was not liked by her mother. Subsequent interviews with the mother verified these impressions. The mother stated that she had never been able to give the child affection and did not feel toward her the way that she felt toward the other children. The patient was like her father, and there were many things about the father which the mother "could not stand."

The attitude of the mother, together with the patient's fear of her father, were the reasons for her deep-seated insecurities. She dreamed that skeletons or ghosts were going to kill her with a knife or, sometimes, choke her. The skeleton or ghost was usually her father. The first attack occurred when she had such a dream. Terrified, she rushed to her mother's bed and grabbed her mother by the arm. Her mother had a painful, swollen elbow at the time; she awoke and slapped the child in the face, whereupon the girl felt that she was choking, rushed to the window and had trouble in breathing for about half an hour. The following day she had a similar attack.

The patient felt that she was very bad. She never did anything wrong but had intense resentments toward both parents and felt guilty about these feelings. She believed that people got sick and died when they were bad. Her mother put her hand to her throat and seemed to choke when the parents "got mad and had fights." The patient often felt scared; she then imagined that she would get sick and die, and the choking spells developed.

The disturbance in this case is typical of that in an adult anxiety neurosis, in which the patient feels scared and brings on a panic by imagining that terrible things will happen. The child was scared because of her insecurity with regard to her parents—because she was not liked. One can see that specific fears caused the panics. Although conditions of this kind are uncommon in children, they are frequently encountered in adults. This case is important because it indicates the factors contributing to the psychologic maladjustments of adults. Less severe but similar conditions are found in all those children who are destined to become "nervous" adults.

Icterus Gravis Neonatorum. Dr. M. I. Vinnecour.

The patient was born on Jan. 14, 1941 at about 2 a. m. I saw her the following morning, about eight hours after birth, at which time she was remarkably pigmented, being almost orange. The spleen was about 4 cm. above the costal margin; I could not make out the liver, because it was below the iliac crest. The blood count at birth showed 3,800,000 red cells per cubic millimeter, of which 29,000, by actual count, were nucleated, and a hemoglobin content of 90 per cent. A blood transfusion was attempted, but a vein could not be isolated; so the blood was given intramuscularly. The next day the red cell count was 3,600,000 per cubic millimeter of blood, and 80 cc. of citrated blood was given intravenously. The erythrocyte count rose to 4,200,000 and then started to drop again. Again a transfusion was given, and the blood count remained constant for four days; then it dropped, and a fourth transfusion was given. During this time liver extract, given intramuscularly, and vitamin K were administered three times a week. Iron was also given, at first orally and then intramuscularly. After each transfusion the erythrocyte count would remain elevated for a longer period. Finally, in order to conserve the vein, intramuscular administration of blood was tried, and the response was almost as satisfactory. Each time that 20 cc. of blood was given intramuscularly the red cell count remained elevated for a little longer before it dropped, and now she is getting along without receiving any more blood. The reticulocyte count was as high as 6 per cent. The liver gradually receded in size, as did the spleen, until they are now barely palpable. She is still slightly icteric.

It is suggested that in cases of icterus gravis neonatorum, after the rate of destruction of the red blood corpuscles has diminished, intramuscular injections of whole blood be given to increase the erythrocyte count.

Slipped Upper Femoral Epiphysis. Dr. Charles N. Pease.

All physicians are familiar with the old treatment of slipped upper femoral epiphysis, that is, reduction by manipulation and application of a cast. The usual results have been poor in that a stiff hip often results.

In this case the method used was reduction of the dislocation and insertion of a Smith-Petersen nail, followed by active and passive motion, thereby establishing a more normal condition in the hip joint and the extremity.

The patient, a 12 year old girl, stepped into a hole, twisted the right leg and fell. It was necessary for her to be carried to the hospital. She had had a slight limp on the right side for three weeks prior to the accident. The past history was irrelevant except for osteomyelitis of the tibia a year before.

The first slide shows the neck of the femur almost completely dislocated from the capital epiphysis. The second slide shows accurate reduction of the head of the femur, fixed by means of a Smith-Petersen nail inserted through the neck of the femur. At the time of operation the joint capsule was found to be torn. A specimen taken for biopsy showed a long-standing inflammatory process, which consisted of arteriolar endarteritis, hyalinization and round cell infiltration.

The child left the hospital, on crutches, in a month. All motions about the right hip joint are as good as those about the left. She walks without any support. The gait is normal.

Actinomycosis. Dr. Wesley Nock.

Case 1.—The patient was admitted with the history that about four and a half months before she had been operated on for a ruptured appendix. Two months later she was discharged, with a fecal fistula. This was treated with silver nitrate cautery and seemed to be improved until one week prior to admission to Children's Memorial Hospital, when it became more irritated and required fifteen to twenty changes of dressing daily.

On admission the fistula, which was over McBurney's point, was injected with iodized poppyseed oil, and a roentgenogram showed the oil running into the small bowel close to the abdominal wall. All attempts to close the fistula proved unsuccessful until it was closed surgically. The patient was discharged in two weeks.

Thirteen months later she was readmitted. Examination showed a hard superficial mass about the size of a lemon around the appendectomy scar. The abscess was opened, and 10 cc. of pus was obtained. The wound continued to drain, and two weeks later it was explored. The peritoneum was intact. A specimen of pale granulation tissue was removed from the abdominal wall and sent to the laboratory. A report of actinomycosis was returned. The wound continued to drain. Sulfanilamide powder was used locally, and within eight days the wound was dry.

Sixteen days later the patient was readmitted with the complaint that the wound was again inflamed and painful. Examination showed a draining sinus, with redness and tenderness over the area. Sulfanilamide powder was again applied to the wound, and 1 grain of the drug per pound (0.06 Gm. per 0.5 Kg.) of body weight was given daily by mouth. The wound healed within a week; the oral administration of sulfanilamide was continued for twenty days. Throughout the course the temperature remained normal except on two occasions, once when the throat showed redness and a second time when the patient had measles.

During the two months since the last episode there has been no recurrence of the fistula.

Case 2.—The patient, a boy, was admitted to the hospital in June 1940. Six months prior to admission he complained of severe pain in the right side and the back. For two months prior to admission the temperature had been elevated. One month later there was a swelling of the side, which subsided and recurred.

A large, dome-shaped, tender area, 4 inches (10 cm.) in diameter, was observed below the right scapula. This was opened and a moderate amount of pus was obtained, which on culture yielded Streptococcus haemolyticus. Sulfanilamide was given by mouth for two weeks, with no effect on the drainage. Another abscess of the chest wall, which developed a month and a half after admission, was drained, and this was followed by several others in the same region. Various forms of treatment, roentgen therapy, local applications of potassium permanganate and silver nitrate and administration of potassium iodide and thymol, were unsuccessful.

Three months after admission a bronchoscopic examination was made, and the aspirated material was reported to contain Actinomyces bovis; this organism was also found in the material from the abscesses. The lesions seemed to clear up to some extent with the use of thymol packs locally and the administration of thymol by mouth, but new abscesses continued to form.

Six months after admission, sulfanilamide was again given orally for three weeks, and then the administrations were stopped because of the lowered leukocyte count. Three transfusions were given, and the drug was again administered. There have been no new abscesses, and the old ones are entirely healed.

Leptothricosis. Dr. Wesley Nock.

The patient was admitted in April 1939, with a history of cough and pain in the right side of the chest when laughing and loss of weight. The patient had been in the hospital eight months before with postinfectious nephritis, and shortly before discharge she had had some tonsil tags and her adenoids removed. Ten days afterward the cough and pain started.

On admission there was some bronchial breathing and bronchophony over the upper lobe of the right lung, and a roentgenogram showed clouding in this area. The temperature was elevated to 100 F.; the leukocyte count was 24,800; the urine was normal, and the Mantoux test gave a negative reaction.

Several bronchoscopic examinations showed that the right main bronchus was red and full of thick white pus. The patient was discharged in one month, to be followed up in the outpatient department.

In May 1939 she was readmitted because of the continued cough, night sweats, poor appetite, loss of weight and low grade evening temperature. At this time there were dulness and suppression of breath sounds over the upper lobe of the right lung. The temperature was 102 F. but soon returned to normal. The leukocyte count was 40,200; the urine was normal. Bronchoscopic examinations were made every five or six days. Examination of pus on several occasions showed gram-positive filamented, nonseptate, unbranched forms, which resembled Leptothrix. There was little improvement, and in August a diagnostic lung puncture was made, which yielded material containing Leptothrix. Administration of potassium iodide in large doses over the next three weeks resulted in no improvement. Neoarsphenamine, sulfanilamide, sulfapyridine (2-[paraaminobenzenesulfonamido] pyridine) and thymol were also used without benefit.

The patient's course continued downhill, and in December the entire right side of the chest appeared to be involved. Vomiting was frequent, and clubbing of the fingers was evident. From November 1939 to June 1940, the temperature showed a daily rise to between 100 and 103 F. During this period the patient lost 37 pounds (16.8 Kg.). Several times organisms resembling Leptothrix were found on direct smear. During the latter part of 1940 cavitation appeared in the upper lobe of the right lung. The patient contracted chickenpox in November 1940.

During December some improvement was evident, for no apparent reason. There was less coughing and vomiting. She gained 10 pounds (4.5 Kg.) in a little over a month. Roentgenograms of the right side of the chest showed marked cavitation over the entire right side. She now weighs 50 pounds (22.7 Kg.), vomits only occasionally and has little cough. If this improvement continues, right pneumonectomy will be considered.

Cerebellar Abscess. Dr. Douglas Buchanan.

The patient, a 6 year old girl, had an infection of the upper respiratory tract, with otitis media, in November 1940. Drainage of the ear, which began spontaneously, continued for three days and then stopped. She was in bed for three weeks and did not recover completely. She again had a cold in the head, was feverish and ill and remained in bed through December and January. Early in February she was taken to a hospital, where a diagnosis of tuberculous meningitis was made. The spinal fluid contained an unknown number of white cells. The

spinal fluid and the blood showed a 4 plus Wassermann reaction. Antisyphilitic treatment was given for a week, and then discontinued because of vomiting. Examination showed that the spinal fluid still contained an unknown number of cells, but the Wassermann reactions of the spinal fluid and the blood were negative.

She was transferred to Bobs Roberts Memorial Hospital for Children not for diagnosis but because she appeared to be dying. There were a papilledema of 5 D., complete paralysis of the right abductus muscle, a right cerebellar syndrome and nystagmus, and it was thought that she had an abscess of the right side of the cerebellum.

At operation a large quantity of pus was found. No attempt was made at that time to drain the abscess, but a week later the entire abscess cavity was drained. During both the needling and the open operation sulfapyridine was given. At the end of the week, when operation was performed, the pus in the abscess contained 8 mg. of sulfapyridine per hundred cubic centimeters.

After the operation there was some improvement, but the complete paralysis of the right external rectus muscle remained. A roentgenogram did not demonstrate any air cells which could contain pus, and it was thought that a daughter abscess had budded from the original focus. Through the drain, which was still in place, 3 cc. of iodized poppyseed oil was injected and it was found that this presumption was correct. The daughter abscess was drained, and the child is now comparatively well. There is still definite ataxia, but the prognosis appears to be good.

Arthrogryposis. Dr. Ferdinand Seidler.

So far only 52 cases of this condition have been described in the literature. Arthrogryposis is not a good name, as it means "curved joints" while in this disease some are rigid in complete extension. Arthrogryposis is not primarily a disease of the joints; some of the muscles either do not form at all or degenerate in early embryonic life and are replaced by fatty fibrous tissue. The joint may be of abnormal shape. Strong fibrous bands or masses of fibrous tissue fill the joint spaces. It is not a spastic condition, and there is normal electric reaction. The joints do not respond to the usual treatment employed for spastic contractures. Even if the muscles are entirely cut away the joints still do not move. The joint must be opened wide to cut out the fibrous tissue.

In this case extensive operations and careful histologic examinations were carried out. The child was in typical position: The arms were close to the body, completely rotated inward; the knees were extended, and the feet were in extreme equinovarus position. Manipulation was first attempted, with little success, and then surgical procedures were started. She can now walk, without much motion in the knees. The hand is more useful, with the elbow flexed and the wrist straight. The wrists were straightened by removing all the carpal bones, which were one mass of bone with only islands of cartilage and no real joints. The triceps were weak, but one was transplanted to replace the biceps, and a flexor was made of it, gravity being used to effect the extension. The next step will be an arthrodesis of the shoulder in elevation. The child is still exercising the arms.

Chronic Nephritis. Dr. H. H. Boyle.

The patient, a boy aged 33 months, had two conditions which were probably not related. He was admitted to Children's Memorial Hospital on Dec. 31, 1940. Two months before his mother had noted a swelling of the left side of the scrotum, which she thought receded at night and became larger in the daytime. At that

time there was no pain or fever. Then she noticed a swelling of the face, particularly about the eyes, which gradually became more pronounced, and generalized edema developed. Two days before admission there was a rather sudden onset of fever and vomiting. The scrotum was red, tender and tense. The temperature was 103 F. (rectal), the leukocyte count was 40,500 and the scrotum was about the size of a large orange on admission. Examinations then and since showed that the urine contained albumin 4 plus, and there is more or less constant edema. The specific gravity of the urine has been about 1.020. Examination has shown 49.5 mg. of nonprotein nitrogen per hundred cubic centimeters of blood. There is no history of acute infection preceding the onset of edema.

At the time of admission the mass in the scrotum presented a problem. It was decided not to operate. There has been no fever since January. Dr. K. E. Barber, a consultant in the urology service, advised the use of support and hot wet dressings. His impression was that the mass was due to torsion, tumor or abscess of the testicle. He advised a roentgen examination of the chest to determine whether tumor metastases were present. The results of the roentgen examination were negative. Aspiration of the mass gave only a few drops of material, which on culture yielded Pneumococcus type VI. Because of the nephritis it was felt that it would not be wise to administer sulfapyridine.

The swelling gradually subsided, and the scrotum now appears normal externally. Dr. Barber has expressed the opinion that there are now two distinct masses in the left side. One is the normal testicle, in normal position, and above that is a smaller mass, apparently scar tissue from the abscess. He has expressed the belief that there is no further measure to be considered, from the urologic standpoint. The nephritis is still present.

Effect of Testosterone Propionate and Alpha Estradiol Benzoate on the Function of Normal Testes. Dr. Norris J. Heckel.

The first slide shows a photomicrograph of a specimen of testis taken for biopsy after the administration of testosterone propionate, which had been given to the patient for its possible effect on an enlarged prostate gland. It shows the extensive destruction of the seminiferous tubules. In other words, this patient was made sterile by the administration of this material.

The next picture shows a photomicrograph of a specimen of testis taken for biopsy after the administration of alpha estradiol benzoate, which had been given for its possible beneficial effect on an enlarged prostate gland. The same destructive changes in the seminiferous tubules are seen here as in the first slide.

Since such harmful changes occur in the adult testis, it is logical to assume that they may be equally extensive in the testis before puberty. Therefore, a word of caution must be given against the promiscuous use of such preparations in the treatment of young boys.

Chondromatosis of the Hip Joint. Dr. Fremont A. Chandler.

The patient came to Children's Memorial Hospital because of pain of several weeks' duration involving the area of the left hip. There was no definite history of injury or acute infection. The pain was localized in the hip joint, with some radiation to the left knee. The general history was essentially noncontributory. No abnormalities were noted in the blood picture. Tuberculin and Wassermann tests gave negative reactions.

Roentgenograms of the left hip showed some atrophy of bone and definite widening of the joint space between the base of the acetabulum and the calcified bones of the head of the femur, which made the head of the femur appear to be dislocated laterally. Motion of the hip joint was through an entirely normal range in all directions. There was no acute pain or tenderness, no elevation of

temperature and no real spasm. The apparent distention of the capsule warranted exploration of the hip joint.

The capsule was opened anteriorly, and a large mass of rice bodies, numbering 324, extruded into the wound. These were removed carefully; although the hip was thoroughly explored, no source of the rice bodies was revealed. The joint was closed, and the patient made an uneventful recovery.

Hidrosis of the Right Leg, Secondary to Neuroma of the Femur. DR. FREMONT A. CHANDLER.

The patient entered Children's Memorial Hospital with a complaint of profuse sweating of the right foot and leg. She had been under observation in various departments of the hospital for several months, without a definite diagnosis being made, prior to being referred to the orthopedic department.

The girl, who was about 10 years of age, had very profuse sweating of the right lower extremity. Both the stocking and the shoe on that side were saturated, while the left extremity was entirely dry. Since this appeared to be a reflex phenomenon, a search was made for a possible sympathetic tumor or a congenital defect of the lower portion of the spine.

Roentgenograms of the spine, the pelvis and both lower extremities were made. The results of the neurologic examination were entirely negative. A roentgenogram of the right femur was normal except for an area of rarefaction involving the cortex just distal to the lesser trochanter. The cortex over this area was slightly thickened and had the appearance commonly associated with osteoid osteoma. This area was excised and the remaining defect filled with bone chips. Sections made of the excised area showed definite nerve trunks, and a diagnosis of neuroma involving the cortex of the femur was made.

It was interesting to note that sweating of the extremity subsided entirely and has not recurred since removal of the tumor mass. In all probability the tumor was a nerve rest which was incorporated in the cortex; in some way a reflex mechanism was set up which caused the sweating. This case is unique in my experience.

Multiple Foreign Bodies in the Esophagus. DR. PAUL HOLINGER.

The patient, a girl aged 18 months, was brought to the hospital because of difficulty in swallowing. Her mother had removed an open safety pin from her mouth and thought that she might have swallowed another and that it had produced the dysphagia. Roentgenograms showed numerous foreign bodies throughout the gastrointestinal tract. The upper thoracic portion of the esophagus contained four interlocking open safety pins, and two uniform buttons were located above the safety pins, one of the buttons having the stud attached. A barrette was noted in the colon.

When admitted, the child had a temperature of 100.4 F. During an esophagoscopic examination the two buttons were removed with the technic usually employed for handling flat foreign bodies. Further roentgenograms taken to study the positions of the point branches of the four pins revealed that two pointed to the right and two to the left. It was observed that the smaller pin was uppermost and should be removed first. This pin was embedded in the mucosa and apparently had been there for a number of weeks. It was removed by the straightening method, as was the second pin on the same side. The two pins whose points were toward the left were entangled, the keeper branch of one being tangled with the keeper of the other. They were taken to the stomach, disentangled and removed. The entire procedure was carried out under the biplane fluoroscope, with a total roentgen exposure of nine minutes, or 45 r, to the back of the chest and one minute, or 5 r, to the left lateral thoracic wall.

The following day the child passed the barrette clamp and four small celluloid objects in the stool. Her temperature returned to normal, and she was discharged on the second postoperative day.

This case is interesting because of the number of foreign bodies in the esophagus and the minimum of symptoms they produced. Without a doubt at least one of the pins had been in the esophagus for weeks. So far as the buttons were concerned, the mother remembered that they had been on the table the day before the child was admitted; so they were of recent origin.

In a series of over 300 cases of foreign bodies in the esophagus, the open safety pin has been the greatest offender. In this instance, the child herself could never have reached the pins. Her brother, a year older, had reached them by climbing onto the dressing table, where they were placed, open, in a pincushion.

Intestinal Obstruction Due to Richter's Hernia. DR. ALBERT H. MONTGOMERY.

Recently, I have seen 2 infants who had symptoms of acute intestinal obstruction. The first was a 5 week old boy who had been vomiting for two days. A small tumor mass was noted in the right groin and was thought to be a hydrocele, because it was translucent and not hard. A roentgenogram was taken with child in the erect position. It is well known that the small bowel normally does not contain gas visible on roentgen examination. When gas is visible it is indicated by mirror lakes (film), which are fluid levels produced by liquid in the bowel. Such lakes are practically pathognomonic of intestinal obstruction.

The child was operated on, and during the manipulation of the bowel to find the point of obstruction a roughened, inflamed area was found on the antimesenteric border of the lower part of the ileum. This was evidently the point of obstruction, because after it was released the collapsed bowel began to fill. Nothing further was done, and the abdomen was closed. It was then noticed that the inguinal mass had disappeared. Evidently the mass was a Richter hernia, in which only a portion of the lumen of the bowel was incarcerated in the hernial sac, and obstruction had been produced by kinking at that point.

Shortly after this a 2 month old infant was brought to the hospital because of vomiting for two days. There was a mass in the right inguinal region, which was thought to be a hernia. A roentgenogram taken with the infant in the upright position showed the fluid level mirror lakes in the small bowel (film) that are present in cases of obstruction.

Although Richter's hernia is a well known pathologic entity, it is a relatively uncommon condition. However, it is an old clinical experience that if one sees one patient with a peculiar condition another will be observed very shortly. When the second patient came in, the house officer was a little more experienced and by manipulation reduced the hernia. The baby, who had not passed anything by the bowel for several days, immediately began to pass flatus and stools and was cured.

Acute Septic Pemphigus. DR. MILA PIERCE, Evanston, Ill., and DR. J. R. WEBSTER.

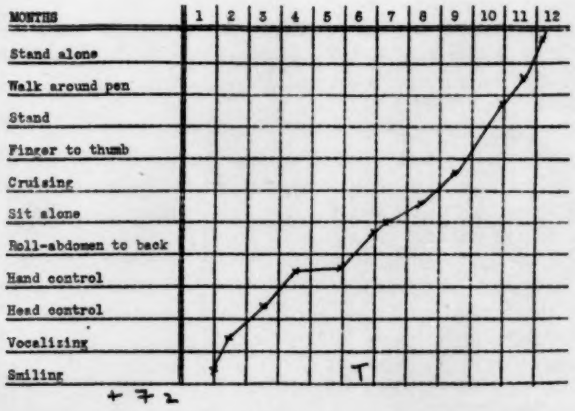
The patient was a 13 month old girl. Photographs were shown and the clinical course and the postmortem observations discussed.

DISCUSSION

DR. J. R. WEBSTER: From the standpoint of the dermatologist this was a most interesting and unusual case, since we were unable to find any instance in the literature of association of this clinical dermatologic picture and leukemia

and there are very few cases of this disease in which the patient was so young. Cases have been reported in which the disease followed vaccination, but they are very few, and the patients were mostly older children. In spite of these unusual facts there can be little doubt that this cutaneous eruption should be placed in the class of acute septic pemphigus, which is an entity distinctly different from ordinary pemphigus. It is to be regarded as a surface expression of an overwhelming toxemia due to an infectious process; it is a rapidly progressive disease which usually ends fatally in a short time.

During our short observation of the cutaneous condition in the hospital, we noticed two or three fairly significant facts. Dr. Pierce mentioned the surprising ease with which the superficial layers of the uninvolved skin could be rubbed off. The mechanism of this is not completely understood, but it is something which affects the entire cutaneous surface and is characteristic of the diseases of the pemphigus group. The other significant facts which we noted were that bullae appeared spontaneously on clinically normal skin and, finally, that the application to uninvolved skin of some such simple thing as alcohol resulted in the formation of superficially placed bullae.



Neuromuscular development of the child to the age of 1 year.

So far as differential diagnosis is concerned, two disorders must be considered; one is bullous impetigo, sometimes called pemphigus neonatorum, and the other is dermatitis exfoliativa neonatorum, or Ritter's disease. I do not propose to enter into a discussion of whether these two diseases are basically the same disorder. The fact remains that the differentiation of the disease in this case from those two entities rests mainly on the more or less generalized solution of the intimate continuity between the epidermis and the corium, a phenomenon usually referred to as the Nikolsky sign, and the appearance of bullae on clinically noninflamed skin, either spontaneously or subsequent to trifling chemical or physical irritation.

Neuromuscular Development to the Age of One Year. Dr. C. Anderson Aldrich, Winnetka, Ill.

A graph is presented to demonstrate the neuromuscular development of the child up to 1 year of age. The advantage of this graph over previously published charts is that it requires no apparatus for establishing the maturation points of development. It is suggested that such a graphic demonstration in the first year of life may afford an accurate way of making a more definite prognosis as to the mental and physical efficiency of a child.

Book Reviews

Das Vitamin K und seine klinische Bedeutung. By Dr. Fritz Koller. Price, 6.75 marks. Pp. 151, with 15 illustrations. Leipzig: Georg Thieme, 1941.

There are a great many problems concerned with the clinical use of vitamin K which still remain unsolved, but there are enough data accumulated to justify a monograph of this type, which summarizes present knowledge. The author shows not only a comprehensive knowledge of the literature in this field but personal experience born of careful laboratory investigation and clinical observation. The monograph covers every aspect of vitamin K.

In the opening chapter the history of the discovery of vitamin K is related, and the work of Dam is cited as having laid the groundwork for the isolation and chemical identification of vitamin K. Other contemporary work is also reviewed. In the next chapter the author discusses the quantitative determination of vitamin K by the indirect methods for measuring prothrombin clotting time. The preventive methods of Almquist and others are briefly sketched, and the question of expressing the values in units is discussed. Koller brings out the practical point that the use of vitamin K units is necessary to express the vitamin K content of such things as plants, dietary materials and animal organs, but that for therapeutic purposes such unitage is no longer of value because in general the dose is measured in milligrams of the synthetic material administered. However, for comparison of the different derivatives in relation to their biologic activity it is necessary to express the values in units. A summary of a table, constructed by the author, on the unitage of various plants shows that green plants have the highest content of vitamin K. A table on the vitamin K content of organs is also appended. The chemistry of vitamin K and its derivatives is next discussed.

In the succeeding chapter the physiology of coagulation in relation to vitamin K is considered, and the author points out that vitamin K is not simply a unit within the structure of prothrombin and gives evidence for such reasoning. He concludes that vitamin K acts on the liver as a stimulus for the formation of prothrombin. The various methods for prothrombin determination are discussed in detail, and, like most workers in this country, the author prefers the method of Quick for use with older children, on whom phlebotomy can be performed. In the method of Fiechter, which the author prefers for use with smaller children, capillary blood is utilized, and the procedure is essentially a microadaptation of Quick's method and is similar to the microtechnics in use in this country. Its practical value at the bedside is limited, however, by the fact that a water bath to hold the temperature of the material constant at 38 C. must be used. The normal value by this method is fifteen to eighteen seconds, as compared with the value for Quick's macromethod, in which plasma is utilized, of twelve to fifteen seconds.

The remainder of the monograph is concerned with the clinical applications of vitamin K. In his discussion of the prothrombin clotting time in cases of obstructive jaundice, Koller states that, in order to rule out a fibrinogen deficit, he and his associates have determined the fibrinogen content of the blood gravimetrically and found normal values. Accordingly, he expresses the belief that if adequate doses of vitamin K are used in a case of obstructive jaundice and there is no rise in prothrombin clotting time the diagnosis of uncomplicated obstructive jaundice is greatly in doubt. He concludes, as have others, that the hypoprothrombinemia in cases of obstructive jaundice is due to exclusion of bile from the intestine, with consequent deficient absorption of vitamin K. In support of this contention he cites a case in which a biliary fistula was present and the hemorrhagic

manifestations were cured by feeding the patient his bile. The author's observations on sprue and celiac disease check with those reported in the literature.

The relation of vitamin K to diseases of the liver parenchyma are considered next. Many of these interesting data are summarized in tabular form. Koller proposes the administration of vitamin K as a test of hepatic function and gives his technic for the procedure, in which a water-soluble preparation of vitamin K is used. However, as the author appreciates, the test assesses only one of the many functions of the liver, and the test is of value chiefly when surgical intervention is being considered.

A large section is devoted to hemorrhagic disease of the newborn. The occurrence of physiologic hypoprothrombinemia in normal infants is corroborated, and the successful use of vitamin K in cases of bleeding is reported. The aiming of prophylaxis directly at the infant and indirectly at the mother is discussed. The experience of the author was that those infants who received vitamin K indirectly, that is, through its administration to the mother before delivery, did not respond as successfully as the infants who were given vitamin K directly. This observation is at variance with the results of similar studies reported in this country. The controversial points with regard to the causation of physiologic hypoprothrombinemia are next considered, and the author reaches the same conclusion that has been expressed by many American investigators, namely, that, besides vitamin K deficiency, hepatic insufficiency plays a part. Contemporary contributions on this subject, both American and European, are reviewed. In concluding the monograph, the author proposes a pathogenetic classification of hemorrhagic diseases.

The monograph is a comprehensive summary of the entire subject and is well done. It is well written, simple in style and well documented with pertinent data. A refreshing feature which is often missing from European monographs is the judicious review of contemporary American contributions.

The Story of Clinical Pulmonary Tuberculosis. By Lawrason Brown, M.D. Price, $2.75. Pp. 411. Baltimore: The Williams & Wilkins Company, 1941.

The title of this book is somewhat misleading. The more so, perhaps, because one associates the name of Lawrason Brown with modern phthisiology and so expects a book written by him to be the story of present day concepts of tuberculosis. Actually, however, the book is the history of clinical pulmonary tuberculosis. It is based on notes which Dr. Brown used in his capacity as lecturer in the Trudeau School of Tuberculosis. Although it had long been his plan to write such a book, his health failed, unfortunately, and he died before he could carry out his intentions. But his wife and his intimate associates joined in completing the task.

One is impressed by the tremendous amount of historical research the author must have done in marshaling his facts. Not only does he mention the names of all the prominent physicians of a period whose writings and words contributed to the knowledge of tuberculosis, but he is at pains to establish for the reader the contemporary background as reflected in the political, social and economic life of the times.

Essentially the book is concerned with describing the origin of percussion, auscultation, roentgenography and thoracic surgery and the influence these discoveries have had on the diagnosis and the treatment of tuberculosis. Perhaps the most interesting chapters are those which deal with Laennec and his discovery of the stethoscope. At that time (1820) the center of medical knowledge was in Paris, and one is astounded to learn that it was the custom to begin ward rounds before daylight, that the autopsy rate for patients dying in public hospitals was nearly 100 per cent and that Laennec, with his students, followed diseased patients to the dissecting room, where the attempt was made to correlate the history and the clinical data with the conditions disclosed by the postmortem examination. While Laennec never achieved early diagnosis of tuberculosis with his *pectorilo-*

queur, or stethoscope, in the sense that such early clinical diagnosis is understood today, he nevertheless paved the way for this important achievement by his successors.

Again one is somewhat taken aback to learn that James Carson in 1820, after sound animal experimentation, including induced pneumothorax, actually performed an operation for artificial pneumothorax on 2 patients with tuberculosis.

While the author has indulged in a good deal of repetition, it must be said that he has succeeded in presenting a most interesting, yes, even fascinating, story of the way physicians thought and spoke and the way they acted toward their patients as the drama of the increasing knowledge of tuberculosis unfolded down through the centuries. He describes a visit of a physician to a patient with tuberculosis in 1700, in 1800 and in 1900. He also describes the diffusion of knowledge of tuberculosis in Germany, Austria, England and America and the contributions made by physicians in each of these countries. If the reader's reactions coincide with those of the reviewer, he will be left with a much greater respect for the accomplishments of the medical profession of a century ago than he ever had before.

The Wonder of Life. By Milton I. Levine, M.D., and Jean H. Seligmann. Price, $1.75. Pp. 114, with 37 illustrations. New York: Simon & Schuster, Inc., 1940.

The importance of conveying some knowledge of the facts of life to young people has received increasing recognition in recent years. This little book performs the task well; the language is simple and the diagrams uncomplicated, so that both may be easily understood by young readers. The experimental proof that life is not spontaneously generated is clearly set forth. From this point the text goes on to the description of a cell and cell division and then to the manner of fertilization of the egg in various types of animals. Simple descriptions and diagrams explain the reproductive systems of both men and women. Some readers who have more or less old fashioned ideas may wonder whether any real purpose is served by the extremely frank description of human sexual relations and whether an activity which, in countless ages and in all of animate creation, has gone on efficiently and effectively might not have received a little less detailed delineation.

The chapter on the unborn baby is well done, and the one describing the mechanism of labor, on the whole, is good. The likening of the laboring uterus to a bag of sand on which one presses with the hands to expel its contents is not an apt simile. One may question, too, the statement that the baby's head becomes smaller while being born. The authors mean that some diameters become shorter and some longer but the bulk remains the same. In the paragraph concerning cesarian section one finds the statement that "the great Roman emperor, Caesar, was said to have been born in this manner." Obstetric writers have long since ceased to think that Caesar was born by means of an abdominal section because his mother was known to have been living some years after his birth, which would scarcely have been true had she been delivered abdominally. One may point out, too, that Julius Caesar was never an emperor, but such details would not concern the young readers for whom the book is intended. Twins are discussed and heredity is taken up in the chapter on family resemblance. One may question the diagram of a cell on page 99, which is used to indicate the chromosomes. Chromosomes are within the nucleus of the cell, but in the diagram, which shows no nucleus, the chromosomes float freely in the cytoplasm.

A useful glossary completes the book. It is a simple, easily understood and, on the whole, accurate description of the process of reproduction. Except for the rather too careful account of the initiation of human reproduction, which would interfere with the use of the book in mixed classes, it will be a useful means of instruction of young students in the outlines of reproductive physiology.

O filho do hanseniano em face da infecção leprosa. By Octavio Gonzaga, M.D., Prof. Walter Büngeler, Nelson Souza Campos, M.D., and Fernando L. Alayon, M.D. Price, none given. Pp. 137, with 2 illustrations. São Paulo, Brazil: Estado de São Paulo, 1941.

This is an interesting monograph on children born in a leprosarium.

The number of stillbirths in this institution was 12.3 per cent, a rate lower than that ordinarily attributed to syphilis in this locality. Fifty-five per cent of the children weighed under 3,000 Gm. at birth. The incidence of congenital debility was higher among the children born of mothers with the nodular form than among those born of mothers with the macular form of the disease. The mortality at the end of twelve months was 12 per cent. The causes of death are interesting; in 18 cases death was due to bronchopneumonia, in 1 to purulent meningitis and in 1 to obstetric trauma.

The children apparently developed well after birth and showed no adverse effects of the presence of leprosy in the parents; the teeth and the stature were unaffected, and congenital deformities and multiple degenerations were not noted.

Leprosy in the first months of life is rare, even among breast-fed infants, and the children do not show any special predisposition to development of the disease later. Among 300 children who were born of leprous parents, isolated from the mother immediately after birth and observed up to the age of 13 years, there was no evidence of congenital leprosy. In the opinion of the writers, the children of leprous parents not only have no intrauterine infection but show a special resistance to such infection. Leprosy in a child is frequently of the tuberculoid form with a tendency to cure; the generalized nodular form is rare.

Textbook of Pediatrics. By Dr. J. P. Crozer Griffith and Dr. A. Graeme Mitchell. Price, $10.00. Pp. 991, with 220 illustrations and 66 tables. Philadelphia: W. B. Saunders Company, 1941.

The textbook of Griffith and Mitchell has been completely revised and to a great extent rewritten. In this third edition more space has been given to the discussion of growth and development than in previous editions, and there is included material on mental and emotional, as well as physical, growth for the periods up to and including adolescence. The plan of the book is similar to that followed before. The first part is given over to general subjects—growth, feeding, hygiene, examination of the child, various diagnostic and therapeutic measures and pediatric institutions and organizations. The part on diseases starts with a section on infectious and communicable diseases, which is followed by sections on general nutritional diseases, metabolic derangements and miscellaneous disorders, including poisoning. After this the diseases are discussed according to systems.

The entire text has been written by the authors, but in preparing it they have consulted the numerous authorities in special fields whose names are given in the front of the book. This makes for uniformity of style, clarity, lack of repetition and facility in using cross references. For example, at the place where a subject is mentioned briefly a reference to the page where a fuller discussion is given is cited. Because of the wide range of works consulted it was impossible to give a complete bibliography; so this feature has been omitted. The index gives evidence of careful preparation. The book is to be highly recommended; it is as complete and up-to-date as possible and exceedingly well written.

Bone Graft Surgery in Disease, Injury and Deformity. By Fred H. Albee, M.D. Price, $7.50. Pp. 403, with 297 illustrations. New York: D. Appleton-Century Company, 1941.

This is a book dealing largely with the operative technic used and recommended by the author for bone grafting procedures and is thus limited in scope. Since discussions of the etiologic, pathologic and diagnostic aspects of the conditions in which such procedures are used and comment on other forms of treatment are lacking, the book is unsuitable for the student or the general practitioner, but it is valuable to the surgeon who does any bone work.

Directory of Pediatric Societies*

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
General Secretary: Dr. Kenneth D. Blackfan, 300 Longwood Ave., Boston.
Assistant Secretary-Treasurer: Dr. Charles F. McKhann, University of Michigan, Ann Arbor, Mich.

Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal.
Place: Boston. Time: Postponed indefinitely.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

Argentine Pediatric Society of Buenos Aires

President: Dr. Martin Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

British Paediatric Association

President: Prof. Charles McNeil, 44 Heriot Row, Edinburgh, Scotland.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Nederlandsche Vereeniging voor Kindergeneeskunde

President: Dr. J. H. G. Carstens, Servaasbolwerk 14ª, Utrecht, Holland.
Secretary: Dr. R. P. van de Kasteele, Laan van Poot 340, 's Gravenhage, Holland.
Place: Different places. Time: Three times a year.

Paediatrický Spolok na Slovensku

President: Dr. A. J. C. Chura, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

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*Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

ROYAL SOCIETY OF MEDICINE, SECTION FOR THE STUDY OF DISEASE IN CHILDREN

President: Dr. E. A. Cockayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

SOCIEDAD CUBANA DE PEDIATRÍA

President: Dr. Clemente Inclan Costa, Manrique 48, Habana.
Secretary: Dr. Serafin Falcon Lopez, Calle B No. 356, Vedado, Habana.
Place: Cátedra de Clinica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Jorge Muñoz Turnbull, Av. Alvaro Obregón 186, Mexico, D. F.
Secretary: Dr. Fernando López Clares, Medellín 191, Mexico, D. F.

SOCIEDAD VENEZOLANA DE PUERICULTURA Y PEDIATRIA

President: Dr. Ernesto Vizcarrondo, Venezuela.
Secretary: Dr. E. Santos Mendoza, Venezuela.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. B. Weill-Hallé, 49 Avenue Raymond Poincaré, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue du Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

URUGUAYAN SOCIETY OF PEDIATRICS

President: Dr. Conrado Pelfort, Av. 18 de Julio 1246, Montevideo.
Secretary: Dr. Héctor Mourigan, Av. 18 de Julio 2175, Montevideo.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

Chairman: Dr. Philip M. Stimson, 25 Claremont Ave., New York.
Secretary: Dr. Hugh L. Dwyer, 315 Alameda Rd., Kansas City, Mo.
Place: Atlantic City.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. Richard M. Smith, 66 Commonwealth Ave., Boston.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Place: Statler Hotel, Boston. Time: Oct. 9-11, 1941.
Region I. Place: Philadelphia.
Region III. Place: Hotel Cleveland, Cleveland. Time: May 14-16, 1942.
Region IV. Place: Ambassador Hotel, Los Angeles. Time: April 23-25, 1942.

AMERICAN HOSPITAL ASSOCIATION, CHILDREN'S HOSPITAL SECTION

Chairman: Dr. D. L. Richardson, 593 Eddy St., Providence, R. I.
Secretary: Dr. Joelle C. Hiebert, 299 Main St., Lewiston, Maine.

American Pediatric Society

President: Dr. Edwards A. Park, Johns Hopkins Hospital, Baltimore, Md.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.

Canadian Society for the Study of Diseases of Children

President: Dr. L. M. Lindsay, 815 Medical Arts Bldg., Montreal.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.
Place: Brockville, Ontario. Time: June 14, 1941.

Society for Pediatric Research

President: Dr. George M. Guest, Children's Hospital, Cincinnati.
Secretary: Dr. Mitchell I. Rubin, 1740 Bainbridge St., Philadelphia.

SECTIONAL

Intermountain Pediatric Society

President: Dr. Eugene Smith, 385-24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

New England Pediatric Society

President: Dr. R. Cannon Eley, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. James Marvin Baty, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

North Pacific Pediatric Society

President: Dr. S. G. Henricke, 4215 N. E. Hancock St., Portland, Ore.
Secretary: Dr. J. S. Backstrand, 333 Wyatt Court, Salem, Ore.
Place: Vancouver, B. C. Time: June 21, 1941.

Rocky Mountain Pediatric Society

President: Dr. Donn Barber, 802½–8th Ave., Greeley, Colo.
Secretary: Dr. Kenneth Schmidt, Republic Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7:30 p. m.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. Harvey F. Garrison, 319 E. Capitol St., Jackson, Miss.
Secretary: Dr. Warren W. Quillian, 227 Aragon Ave., Coral Gables, Fla.

STATE

Alabama Pediatric Society

President: Dr. M. V. Adams, 803 Government St., Mobile.
Secretary-Treasurer: Dr. William R. Britton, 4 Catoma St., Montgomery.

Arkansas State Pediatric Association

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

California State Medical Society, Section on Pediatrics

Chairman: Dr. William Belford, 233 A St., San Diego.
Secretary: Dr. John J. Miller Jr., 2398 Sacramento St., San Francisco.

Florida State Pediatric Society

President: Dr. Warren W. Quillian, 227 Aragon Ave., Coral Gables.
Secretary: Dr. George N. Leonard, 605 Lincoln Rd., Miami Beach.
Place: Concurrent with state association meeting at time of convention.

Georgia Pediatric Society

President: Dr. R. C. McGahee, 1345 Greene St., Augusta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. D. C. Darrow, 789 Howard Ave., New Haven.
Secretary: Dr. Joseph L. Hetzel, 103 N. Main St., Waterbury.
Time: Three meetings a year.

Illinois State Medical Society, Section on Pediatrics

Chairman: Dr. Orville Barbour, 331 Fulton St., Peoria.
Secretary: Dr. Craig Butler, 715 Lake St., Oak Park.

Indiana State Pediatric Society

President: Dr. K. T. Knode, 1105 E. Jefferson Blvd., South Bend.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

Iowa Pediatric Society

President: Dr. Morgan J. Foster, 837 Higley Bldg., Cedar Rapids.
Secretary-Treasurer: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.

Louisiana State Pediatric Society

President: Dr. Julian Graubarth, 3431 Prytania St., New Orleans
Secretary-Treasurer: Dr. W. C. Rivenbark, 3503 Prytania St., New Orleans.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Norman L. Hawkins, 11 Public Sq., Watertown, N. Y.
Secretary: Dr. William J. Orr, 135 Linwood Ave., Buffalo.

Medical Society of the State of Pennsylvania, Pediatric Section

Chairman: Dr. John D. Sturgeon Jr., 22 N. Gallatin Ave., Uniontown.
Secretary: Dr. Elwood W. Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Place: Pittsburgh. Time: Sept. 29-Oct. 2, 1941.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. Harry Towsley, University of Michigan Hospital, Ann Arbor.
Secretary: Dr. Leon DeVel, 110 E. Fulton, Grand Rapids.

Mississippi State Pediatric Society

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

Nebraska Pediatric Society

President: Dr. J. C. Iwersen, 236 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. Elmer W. Bantin, 440 Aquila Court Bldg., Omaha.
Place: As announced by Committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NEW HAMPSHIRE PEDIATRIC SOCIETY

President: Dr. MacLean J. Gill, 14 N. State St., Concord.
Secretary-Treasurer: Dr. Ursula G. Sanders, 46 Pleasant St., Concord.
Time: Twice yearly.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Thomas M. Watson, Greenville.
Secretary: Dr. Frederick B. Haar, Greenville.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. Ben H. Nicholson, 301 N. W. 12th St., Oklahoma City.
Secretary: Dr. Luvern Hays, 108 W. 6th St., Tulsa.
Place: Oklahoma Club. Time: 6:30 p. m., fourth Friday of each alternate month from September to May, inclusive.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. R. B. Josey, 1517 Hampton Ave., Columbia.
Secretary-Treasurer: Dr. Wilson Ball, South Carolina State Health Dept., Columbia.

TENNESSEE STATE PEDIATRIC SOCIETY

President: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.
Secretary: Dr. Gilbert Eblen, 611 W. Main Ave., Knoxville.

TEXAS PEDIATRIC SOCIETY

President: Dr. P. E. Luecke, 4105 Live Oak St., Dallas.
Secretary-Treasurer: Dr. John Ashby, 3610 Fairmount Ave., Dallas.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. John M. Bishop, 511 Medical Arts Bldg., Roanoke.
Secretary: Dr. Edwin A. Harper, 301 Rivermont Ave., Lynchburg.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. Theresa O. Snaith, 450 Center Ave., Weston.
Secretary: Dr. Henrietta L. Marquis, 211 Bair Bldg., Beckley.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. J. D. Nourse, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. I. B. Silber, 10465 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. I. Nelles Silverthorne, 170 St. George St., Toronto, Canada.
Secretary: Dr. G. P. Hamblin, 2333 Bloor St. W., Toronto, Canada.

BRONX PEDIATRIC SOCIETY

President: Dr. David Greene, 910 Grand Concourse, New York.
Secretary: Dr. F. E. Chick, 2325 University Ave., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. John A. Monfort, 861 Carroll St., Brooklyn.
Secretary: Dr. Walter Coles, 604–2d St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, August and September.

Central New York Pediatric Club

President: Dr. Frank van der Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Places: Various cities in New York. Time: Third Tuesday of April and September.

Chicago Pediatric Society

President: Dr. James H. Wallace, 715 Lake St., Oak Park, Ill.
Secretary: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

Dallas Pediatric Society

President: Dr. Edgar Loomis, 351 W. Jefferson Ave., Dallas, Texas.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmont Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

Detroit Pediatric Society

President: Dr. Marsh M. Poole, 773 Fisher Bldg., Detroit, Mich.
Secretary: Dr. Donald J. Barnes, 773 Fisher Bldg., Detroit, Mich.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.
Secretary: Dr. Harry Lange, 478 Peachtree St. N. E., Atlanta.
Place: Academy of Medicine, 38 Prescott St. N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. Thomas J. Donovan, 3820 Fannin St., Houston, Texas.
Secretary: Dr. Raymond Cohen, 2300 Caroline St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. John Aull, 1103 Grand Ave., Kansas City.
Secretary: Dr. George Herrman, 1107 Bryant Bldg., Kansas City.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Alonzo Cass, 1908 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Gladys Patric Shahovitch, 3936 Roderick Rd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Sydney Nussbaum, 247 Ocean View Ave., Brooklyn.
Secretary: Dr. Harry S. Bikoff, 850 St. Marks Ave., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., fourth Monday of each month, October to April, inclusive.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. A. A. Trivilino, 88-07–150th St., Jamaica, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144–38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. Harry A. Ong, 1801 I St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. William F. Burdick, 5402 Connecticut Ave. N. W., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., fourth Thursday of every month.

Memphis Pediatric Society

President: Dr. E. C. Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

Milwaukee Pediatric Society

President: Dr. R. P. Schowalter, 411 E. Mason St., Milwaukee.
Secretary-Treasurer: Dr. George H. Wegmann, 2650 W. Hopkins St., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Leslie O. Ashton, 850 Park Ave., New York.
Secretary: Dr. Alfred Langmann, 108 E. 68th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northern California Affiliates

President: Dr. Crawford Bost, 490 Post St., San Francisco.
Secretary: Dr. William A. Reilly, 384 Post St., San Francisco.
Time: Second Thursday of September, November, January, March and May.

Northwestern Pediatric Society

President: Dr. Harold Flanagan, 711 Lowry Medical Arts Bldg., St. Paul, Minn.
Secretary-Treasurer: Dr. George B. Logan, Mayo Clinic, Rochester, Minn.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Oklahoma City Pediatric Society

President: Dr. J. Byron Snow, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Place: Oklahoma Club. Time: Fourth Friday of each alternate month.

Philadelphia Pediatric Society

President: Dr. Philip S. Barba, 222 W. Harvey St., Germantown, Pa.
Secretary: Dr. Aims C. McGuinness, Children's Hospital, 1740 Bainbridge St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to April, inclusive.

Pittsburgh Pediatric Society

President: Dr. E. L. Piper, 3200–5th Ave., Pittsburgh.
Secretary-Treasurer: Dr. Carl Ruder, 646 Washington Rd., Mount Lebanon, Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate month from October to June, inclusive.

Richmond Pediatric Society

President: Dr. Louise Fry Galvin, 214 S. Boulevard, Richmond, Va.
Secretary-Treasurer: Dr. Herman W. Farber, 501 E. Franklin St., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: 8 p. m., third Thursday of each month, except June, July and August.

Rochester Pediatric Society

President: Dr. Herbert Soule, 122 Rutgers St., Rochester, N. Y.
Secretary-Treasurer: Dr. Jerome Glaser, 300 S. Goodman St., Rochester, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee. Time: Third Friday of each month from October to May.

St. Louis Pediatric Society

President: Dr. Max Deutch, 634 N. Grand Blvd., St. Louis.
Secretary-Treasurer: Dr. Peter G. Danis, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society Bldg. Time: First Friday of each month from October to June.

Seattle Pediatric Society

President: Dr. H. L. Moon, 1700–36th Ave., Seattle.
Secretary: Dr. L. Bradford Ostrom, Medical Dental Bldg., Seattle.
Place: College Club. Time: Third Friday of each month from September to June at 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Norman Nixon, 1136 W. 6th St., Los Angeles.
Secretary: Dr. Donald C. Shelby, 3780 Wilshire Blvd., Los Angeles.
Place: Jonathan Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Campbell Harvey, 35 W. Huron St., Pontiac, Mich.
Secretary: Dr. Harry A. Towsley, University of Michigan, Department of Pediatrics and Communicable Diseases, Ann Arbor, Mich.
Time: Autumn, 1941.

Westchester County Medical Society, Pediatric Section (New York)

President: Dr. John B. Ahouse, 27 Ludlow St., Yonkers, N. Y.
Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Rye.
Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October, December, February and April.